EVALUATION OF THE ROLE OF LOCOREGIONAL INTERVENTIONAL THERAPIES IN THE TREATMENT OF HEPATOCELLULAR CARCINOMA

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Dedicated

to

my Family

&

Teachers

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Dr. Philipose Puliyelil Abraham

LIST OF ABBREVIATIONS

APASL	Asian Pacific Association for the Study of the Liver
AASLD	American Association for the Study of Liver Diseases
AFP	Alpha Fetoprotein
AP	Arterial phase
BCLC staging	Barcelona Clinic Liver Cancer staging
BCLC	Barcelona Chronic Clinic Liver Cancer
B-TACE	Balloon occlusion catheters
C-P GRADE	Child-Pugh grade
cTACE	Conventional TACE
CA	Cryoablation
CLD	Chronic Liver Disease
CT	Computed Tomography
CR	Complete Response
CBC	Complete Blood Count
CA	Complete ablation
CEUS	Contrast-enhanced US
DEB-TACE	Drug-eluting beads TACE
DEM-TACE	Drug-eluting microspheres
DWI	Diffusion-weighted imaging
DCE	Dynamic contrast-enhanced
DP	Delayed phase
DFS	Disease free survival
EASL	European Association for the Study of the Liver
HCC	Hepatocellular Carcinoma
HCV	Hepatitis C Virus

HBC	Hepatitis B virus
HIFU	High-intensity focused ultrasound
IRE	Irreversible electroporation
INASL	Indian National Association for Study of the Liver
L-MWA	Laparoscopic Microwave Ablation
LT	Liver Transplant
LR	Liver resection
LRT	Locoregional Therapy
LI-RADS	Liver Imaging and Reporting Data System
LAP	Late arterial phase
LFT	Liver Function Test
LR	Local recurrence
LTP	Local tumor progression
MRI	Magnetic Resonance Imaging
MELD	Model for End stage Liver Disease
mRECIST	Modified Response Evaluation Criteria In Solid Tumors
MELD	The Model for End-Stage Liver Disease
MWA	Microwave Thermal Ablation
NAFLD	Non-alcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
OR	Objective response
OS	Overall survival
OPTN	Organ Procurement and Transplantation Network
P-MWA	Percutaneous Microwave Ablation
PSC	primary sclerosing cholangitis (PSC),
PEI	Percutaneous ethanol Injection

PVE	Portal vein embolozation
PVP	Portal venous phase
PR	Partial Remission
PD	Progressive Disease
p	Probability when the null hypothesis is true
PFS	Progression-free survival
RFS	Recurrence free survival
RFT	Renal Function Test
RFA	Radio frequency ablation
RCT	Randomized Controlled Trial
SD	Stable disease
SPSS	Statistical Package for Social Sciences
TACE	Trans-arterial Chemoembolisation
SBRT	Stereotactic body radiation therapy
TTP	Time to progression
TARE	Trans-arterial Radioembolisation
US	Ultrasonography
UNOS	United Network for Organ Sharing

ABSTRACT

Introduction: Hepatocellular Carcinoma (HCC) is the 5th most common neoplasm worldwide and the 3rd most common cause of cancer related death. Treatment options for HCC is surgery, locoregional interventional therapies (LRT) and systemic therapies.

Aims of Study: To evaluate the outcome of LRT procedures, offered to patients with HCC patients registered under Department of Radiodiagnosis in DMCH, Ludhiana. Assessments were made according to the modified Response Evaluation Criteria in Solid tumors (mRECIST) criteria. Patient stratification and treatment allocation were based on the Barcelona Clinic Liver Cancer (BCLC) staging system.

Materials & Methods: This is a prospective and retrospective study conducted over a period of three years, in which complete data and follow up was available for 28 patients (male 22, female 6, mean age 61 years) who had undergone LRT for HCC were recruited, 13 (46.4%) underwent TACE and 15 (53.6%) had MWA procedures. Their clinical characteristics, biochemical parameters, and imaging studies were documented and evaluated. Statistical analysis was done using SPSS software. P-value < 0.05 was considered significant.

Results: Basic diagnosis in majority of patients was cirrhosis. The predominant risk factor was alcoholism followed by NASH. The patients included were age-gender matched. Child-Pugh (C-P) classification, BCLC staging system for HCC, and MELD score were comparable among both groups.

In overall treatment response at 6 weeks by mRECIST showed complete remission (CR) in 11 (73.3%) in MWA vs. 2 (15.4%) in TACE group. Partial remission (PR) was observed in 2 (15.4%) in TACE group. Stable disease (SD) was recorded in 4 (30.8%) vs.1 (6.7%) and Progressive disease (PD) in 5 (38.5%) vs. 2 (13.3%) patients, in TACE and MWA groups, respectively, with statistical significant of p= 0.016

Evaluation of survival out-come after 6 months post LRT, there were 14 (93.3%) vs. 6 (46.2%) live patients in MWA and TACE group respectively. Death happened in 5 (38.5%) patients in TACE, but only 1 (6.7%) in MWA group. 2 (15.4%) patients were lost to follow up in TACE group. The differences were statistically significant, p = 0. 019

Conclusion: Evaluation of outcome of Locoregional Therapies (LRT), using modified Response Evaluation Criteria in Solid tumors (mRECIST) demonstrated a better prognosis with superior survival outcome in MWA patients than TACE subjects.

Keywords: Hepatocellular carcinoma (HCC); Locoregional Therapy (LRT); Trans-arterial chemoembolization (TACE); Microwave thermal ablation (MWA); mRECIST

TABLE OF CONTENTS

S. NO.	TOPIC	PAGES
I	INTRODUCTION	1-32
II	AIMS AND OBJECTIVES	33
III	REVIEW OF LITERATURE	34-39
IV	MATERIALS AND METHODS	40-43
V	OBSERVATIONS AND RESULTS	44-84
VI	DISCUSSION	85-90
VII	LIMITATIONS	91
VIII	SUMMARY AND CONCLUSIONS	92
IX	BIBLIOGRAPHY	93-111

APPENDICES – I

- PROFORMA
- MASTER CHART

APPENDICES – II

- APPROVAL LETTER OF THESIS PLAN
- THESIS PLAN

LIST OF TABLES

Table No.	Title	Page No.
1.	LOCOREGIONAL THERAPY TECHNIQUES, BENEFITS, AND RISK	3
2.	CHILD-PUGH CLASSIFICATION FOR SEVERITY OF CIRRHOSIS	11
3.	BARCELONA CLINIC LIVER CANCER (BCLC) STAGING SYSTEM	14
4.	LI - RADS CATEGORY CODES RATING NODULES ACCORDING TO LI-RADS	22
5.	TREATMENT RECOMMENDATIONS CCORDING TO BCLC STAGES	28
6.	mRECIST - MODIFIED RECIST [RESPONSE EVALUATION CRITERIA IN SOLID TUMORS]	31
7.	GENDER DISTRIBUTION OF PATIENTS WITH HCC	48
8.	AGE DISTRIBUTION OF HCC PATIENTS AT PRESENTATION	50
9.	METHOD OF IDENTIFICATION OF HCC	51
10.	BASIC DIAGNOSIS OF LRT PATIENTS AT THE TIME OF PRESENTATION	52
11.	RISK FACTORS FOR CIRRHOSIS IN HCC PATIENTS	53
12.	PRESENCE OF HCV AMONG LRT PATIENTS	54
13.	FREQUENCY OF ALCOHOLISM AMONG LRT PATIENTS	55
14.	INCIDENCE OF SMOKING IN STUDY GROUP	56
15.	INCIDENCE OF OPIUM ABUSE IN STUDY GROUP	57
16.	PRESENCE OF ASCITES THE STUDY GROUPS	58
17.	PRESENCE OF ENCHAPHALOPATHY IN LRT PATIENTS	59
18.	ANTIVIRAL TREATMENT FOR LRT PATIENTS	60

19.	COMPARISON OF MEAN (SD) 0F HEMATOLOGICAL AND BIOCHEMICAL PARAMETERS	61
20.	COMPARISON OF PROPORTIONS REGARDING LIVER FUNCTION TESTS IN LRT PATIENTS	62
21.	SERUM AFP LEVELS IN LRT PATENTS	64
22.	CHILD-PUGH CLASSIFICATION OF LRT PATIENTS	65
23.	BCLC STAGING OF LRT PATIENTS	66
24.	MODEL FOR END-STAGE LIVER DISEASE (MELD) OF LRT PATIENTS	68
25.	PROPORTION OF MODEL FOR END-STAGE LIVER DISEASE (MELD) SCORE IN LRT PATIENTS	69
26.	TOTAL NUMBER OF HCC LESIONS BEFORE TREATMENT	71
27.	COUINAUD SEGMENTS FOR LESIONS BEFORE TREATMENT	73
28.	LI-RADS OF ALL LESIONS DOCUMENTED BEFORE TREATMENT	74
29.	LI-RADS OF LESIONS - 6 WEEKS POST TREATMENT	75
30.	TUMOR SIZE BEFORE TREATMENT	76
31.	METASTASIS IN TACE PATIENTS	77
32.	RESPONSE TO TREATMENT AT 6 WEEKS FOLLOW UP BY mRECIST	78
33.	RESPONSE TO TREATMENT BY mRECIST AT 3 MONTHS	80
34.	AMENDED RESPONSE TO LRT BY mRECIST AT 3 MONTHS	81
35.	SURVIVAL OUTCOME IN LRT PATIENTS	82

LIST OF FIGURES

Fig. No.	Title	Page No.
1.	BARCELONA CLINIC LIVER CANCER (BCLC) STAGING SYSTEM	13
2.	INDIAN NATIONAL ASSOCIATION FOR STUDY OF THE LIVER – (INASL)MODIFIED BCLC STAGING OF HCC	15
3.	LI-RADS MAJOR IMAGING FEATURES	23
4a.	DIAGRAM SUMMARIZING LOCOREGIONAL THERAPIES	25
4b.	DIAGRAM SUMMARIZING SYSTEMIC THERAPIES	26
5.	TREATMENT RECOMMENDATIONS ACCORDING TO BCLC STAGE	27
6.	GENDER DISTRIBUTION OF ALL PATIENTS WITH HCC	49
7.	GENDER DISTRIBUTION AMONG TACE AND MWA PATIENTS	49
8.	AGE DISTRIBUTION OF PATIENTS WITH HCCAT PRESENTATION	50
9.	IDENTIFICATION OF HCC IN LRT PATIENTS	51
10.	BASIC DIAGNOSIS OF LRT PATIENTS AT THE TIME OF PRESENTATION	52
11.	RISK FACTORS FOR CIRRHOSIS IN HCC PATIENTS	53
12.	PRESENCE OF HCV AMONG LRT PATIENTS	54
13.	FREQUENCY OF ALCOHOLISM AMONG LRT PATIENTS	55
14.	INCIDENCE OF SMOKING IN STUDY GROUP	56
15.	INCIDENCE OF OPIUM ABUSE IN STUDY GROUP	57
16.	PRESENCE OF ASCITIS THE STUDY GROUPS	58
17.	THE PRESENCE OF ENCHAPHALOPATHY IN LRT PATIENTS	59
18.	ANTIVIRAL TREATMENT FOR LRT PATIENTS	60

19.	SERUM AFP LEVELS IN LRT PATENTS	64
20.	CHILD-PUGH CLASSIFICATION OF LRT PATIENTS	65
21.	BCLC STAGING OF THE CASES	66
22.	MODEL FOR END-STAGE LIVER DISEASE (MELD) OF LRT PATIENTS	69
23.	PROPORTION OF MODEL FOR END-STAGE LIVER DISEASE (MELD) SCORE IN LRT PATIENTS	70
24.	TOTAL NUMBER OF HCC LESIONS BEFORE TREATMENT	72
25.	TUMOR SIZE BEFORE TREATMENT	76
26.	INCIDENCE OF METASTASIS	77
27.	RESPONSE TO TREATMENT AT 6 WEEKS FOLLOW UP BY mRECIST	79
28.	RESPONSE TO TREATMENT BY mRECIST AT 3 MONTHS	80
29.	AMENDED RESPONSE TO LRT BY mRECIST AT 3 MONTHS	81
30.	SURVIVAL OUTCOME IN LRT PATIENTS	82

LIST OF PICTURES

Pic. No.	Title
1.	POST-TACE TREATMENT. NO RESIDUAL TUMOR (A AND B) AND RESIDUAL DISEASE PRESENT (C AND D)
2.	POST MWA TREATMENT CHANGES. NO RESIDUAL TUMOR (A AND B) AND RESIDUAL DISEASE PRESENT (C AND D)
3.	MEASUREMENT OF THE LONGEST TUMOUR DIAMETER IN A TARGET HEPATIC LESION; MRECIST VS. STANDARD RECIST
4.	APPLICATION OF mRECIST ASSESSMENT FOR HEPATOCELLULAR CARCINOMA (HCC)
5a.	CASE 1: PATIENT DIAGNOSED CASE OF HCC PLANNED FOR TACE, CT TRIPHASIC IMAGES
5b.	CASE 1: POST TACE CT TRIPHASIC IMAGING
6a.	CASE 2: PATIENT DIAGNOSED CASE OF HCC PLANNED FOR TACE, CT TRIPHASIC IMAGES
6b.	CASE 2: POST TACE CT TRIPHASIC IMAGING
7a.	CASE 3: PATIENT DIAGNOSED CASE OF HCC PLANNED FOR MWA, CT TRIPHASIC AXIAL IMAGES
7b.	CASE 3: POST MWA CT TRIPHASIC IMAGING
8a.	CASE 4: PATIENT DIAGNOSED CASE OF HCC PLANNED FOR MWA, CT TRIPHASIC IMAGES
8b.	CASE 4: POST MWA CT TRIPHASIC IMAGING

INTRODUCTION

BACKGROUND

Hepatocellular carcinoma (HCC) is a major health problem being the fifth most common neoplasm in the world, the most common primary liver malignancy and third leading cause of cancer-related mortality worldwide.[1] The overall prognosis of HCC involves a complex interplay of baseline clinical staging, underlying liver function, and demographic factors.[2,3] Nonetheless, the 5-year relative survival rate for primary liver cancer is estimated to be 19.6% [4] with a mean survival being reported between 6-20 months.[5]

Efficient management of HCC depends on early detection, the stage of progression of the disease and underlying liver function.[6] HCC surveillance helps to identify early tumors that are amenable to treatment. Global associations, including the American Association for the Study of Liver Diseases (AASLD), European Association for the Study of the Liver (EASL), Asian Pacific Association for the Study of the Liver (APASL), and Indian National Association for Study of the Liver (INASL), advocate a 6-monthly abdominal ultrasonogram for HCC surveillance.[7-9]

A primary predisposing condition of HCC is liver cirrhosis, a consequence of chronic liver injury leading to subsequent regeneration of liver cells and formation of abnormal structural nodules with surrounding fibrosis. Common causes of cirrhosis include chronic viral hepatitis such as hepatitis C virus (HCV) and hepatitis B virus (HBV); metabolic liver diseases such as non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), hemochromatosis, α1-antitrypsin deficiency, and Wilson's disease; alcoholic liver disease; autoimmune diseases such as primary sclerosing cholangitis (PSC), primary biliary cirrhosis (PBC), and autoimmune hepatitis; and environmental factors such as alfatoxins.[10, 11]

Surgical resection and transplantation are the standard first-line treatments for early-stage HCC. Liver transplantation (LT) is the gold standard of treatment, however few patients are able to take advantage

of this option due to social issues, the lack of available livers and/or the frequent late stage of disease at time of diagnosis.[12] Furthermore, up to 25% of those patients meeting initial requirements and listed for transplantation will eventually drop off the transplant list for a variety of reasons, including tumor progression.[13] Recurrence of HCC following LT has been estimated to be 11%-18%.[14]

Surgical resection is considered to be curative but is generally reserved for patients with solitary tumors with preserved liver function. Preserved liver function is defined as absence of clinically relevant portal hypertension (i.e., hepatic venous gradient of less than 10 mm Hg, absence of varices, splenomegaly and a platelet count of more than 100,000/mm3) and normal bilirubin levels. Poor hepatic function is defined as the presentation of hepatic encephalopathy, uncontrolled ascites, variceal bleeding, serum bilirubin > 3 mg/dL, serum albumin < 2.8 g/dL, or prothrombin time prolongation>4 s over the control. Progressive disease was defined based on an increased tumor size and AFP of more than 25%.[15,16]

Unfortunately, most patients do not fulfill criteria for surgery. In a recent comparative study of more than 8000 HCC cases worldwide, less than 10% of patients fulfilled preoperative criteria for resection.[17] Surgery, despite improved techniques, also confers a higher than desirable mortality and morbidity[18] and, despite these risks, recurrence rates remain significant, reported to be as much as 50% at 2 years.[19]

LOCOREGIONAL INTERVENTIONAL THERAPIES (LRTS), AND OBJECTIVE OF PRESENT STUDY

However novel techniques like locoregional interventional therapies (LRTs) have evolved and are implemented with the intention to cure, downstage or provide palliative care. LRTs include ablasive therapies and trans-arterial therapies.

Locoregional therapies utilized to treat HCC and can be subdivided into thermal ablation and intra-arterial therapies. Thermal ablation is notable as the only LRT considered curative in well-chosen patients, being equivalent to surgical resection.[20,21]

Intra-arterial therapies include transarterial embolization (TAE), transarterial chemoembolization (TACE), and transarterial radioembolization (TARE). These latter therapies are considered life prolonging, but ultimately palliative. Intraarterial therapies are also frequently used in a “bridging” fashion to either get patients within transplant or Milan criteria, or to keep them within criteria while they are on the transplant list. [22]

TABLE 1: LOCOREGIONAL THERAPY TECHNIQUES, BENEFITS, AND RISK

LOCOREGIONAL MODALITY	TECHNIQUES	CLINICAL ADVANTAGES	CLINICAL RISKS
TACE Transarterial Chemo embolisation	Drug-eluting beads or conventional delivery	Provides both local embolic and chemotherapeutic effect	PES, biloma, liver abscess, liver failure
TAE Transarterial embolization	Particulate or other embolic agents	Avoids radio and chemotoxicity; less expensive than other embolotherapies	PES, biloma, liver abscess, liver failure
TARE Transarterial Radio embolisation	Y90 microspheres	May be used in early disease with curative intent; intermediate disease can be used to increase FLV to qualify for curative intent surgery; best QoL scores of all options	PRS, RILD, radiation-induced pneumonitis, biloma, liver abscess, liver failure
ABLATION	Radiofrequency	Efficacious as	PAS,

	current, microwaves, or cryoablation	monotherapy for early-stage disease; less morbidity than transarterial therapies	iatrogenic injury, bleeding

TACE: Transarterial chemoembolization; PES: Post-embolization syndrome; TAE: Transarterial embolization; TARE: Transarterial radioembolization; FLV: Functional liver volume; QoL: Quality of life; PRS: Post-radioembolization syndrome; RILD: Radiation-induced liver disease; PAS: Post-ablation syndrome.

Table adopted from: Makary MS, Ramsell S, Miller E, Beal EW, Dowell JD. Hepatocellular carcinoma locoregional therapies: Outcomes and future horizons. World J Gastroenterol. 2021 Nov 21;27(43):7462-7479. [23]

Sequential treatment using locoregional therapies (ablation, arterially directed therapies, external beam radiation therapy) and systemic therapies (sorafenib, durvalumab, lenvatinib, atezolizumab/ bevacizumab) remains the standard of care for patients with unresectable HCC. Combinations of locoregional therapies along with systemic therapies constitute a growing area of interest with the objective of attaining superior therapeutic outcomes.[24]

While surgical resection and transplantation are the cornerstone of therapy in early-stage hepatocellular carcinoma, locoregional therapy and sorafenib are beneficial in those with more advanced disease or those who are not surgical candidates. At times, the integration of both surgical and locoregional therapy may be necessary. Hence, hepatocellular carcinoma requires a multidisciplinary approach to determine the most appropriate treatment as well as the timing of various treatments for optimal outcomes.[25]

This study was proposed and implemented to evaluate two locoregional interventional procedures offered to HCC patients in our institute.

LOCOREGIONAL THERAPIES (LRTS) USED IN THE PRESENT STUDY

Locoregional therapies for HCC are the most common method utilized to treat HCC and can be subdivided into thermal ablation and intra-arterial therapies. LRT represented by ablation and Trans-arterial chemoembolozation (TACE) has become the main means for the clinical treatment of unresectable HCC. Intra-arterial therapies include transarterial embolization (TAE), transarterial chemoembolization (TACE), and transarterial radioembolization (TARE). These latter therapies are considered life prolonging, but ultimately palliative. Intraarterial therapies are also frequently used in a “bridging” fashion to either get patients within transplant or Milan criteria, or to keep them within criteria while they are on the transplant list. [22]

Thermal ablation is notable as the only LRT considered curative in well-chosen patients, being equivalent to surgical resection.[20,21]Patients with intermediate HCC can differ widely in terms of their liver function, tumour size, and tumour number.[26] Despite this heterogeneity, however, transarterial chemotherapy (TACE) is currently the standard recommendation by most international guidelines for intermediate HCC group of patients.[27,28]

Percutaneous ablative therapies are a viable option in patients which present with solitary nodule less than 5 cm or up to 3 nodules less than 3 cm, showing promising results and are also employed in tumors that are deemed unresectable due to higher disease burden and comorbidities. Radiofrequency is the mainstay for local ablation at early stages and transarterial chemoembolization (TACE) remains the standard treatment for intermediate-stage HCC (multinodular liver-only disease in asymptomatic patients with compensated liver function leading to median survivals of 25–30 months.

TRANSARTERIAL CHEMOEMBOLIZATION (TACE)

TACE is commonly used in patients with unresectable HCC with preserved liver function.[29-31] TACE is widely used in patients with HCC who are not candidates for curative treatments. The BCLC guidelines

recommend transarterial chemoembolization (TACE) as the standard first-line treatment for intermediate HCC without vascular involvement due to its demonstration of consistent survival benefits in BCLC stage B patients.[29]

Intraarterial therapies are centered on the principle that hepatocellular tumors mainly recruit hepatic artery branches for growth whereas normal liver parenchyma receives dual blood flow primarily via the portal vein.

The goal of transarterial embolization (TAE) is to restrict hepatic artery blood flow to vessels supplying a tumor. This causes ischemia-induced cellular membrane disruption and oncosis resulting in ischemic cell death.[32- 34]

Again, the rationale for catheter directed local regional therapies in the treatment of HCC is predicated on the fact that there is a mismatch between blood supply to normal hepatic parenchyma and HCC lesions. Normal liver parenchyma receives ¾ of its blood supply from the portal vein with the remaining ¼ arriving via the hepatic artery. In contrast, advanced HCC derives the bulk of its blood supply from the hepatic artery.[33]

Some HCC lesions are fed by multiple (small) arteries originating from central vessels and are therefore difficult to treat without damaging large portions of the liver. Furthermore, it is frequently impossible to predict arterial supply completely from pretreatment imaging.[35]

Conventional TACE (cTACE) commonly delivers an emulsion of lipiodol and chemotherapeutic agent (most often doxorubicin or cisplatin) followed by gelatine sponge as the embolic agent. However, there is considerable variation in technique and drug mixture across institutions, and pharmacokinetic analysis revealed that plasma concentration after c-TACE may approximate systemic chemotherapy drug levels.[36]

The most recent drug-eluting beads (DEB) TACE utilizes drug-eluting beads preloaded with the chemotherapeutic agent, with a reported reduction of drug-related side effects due to a better pharmacokinetic profile .[37,38]

Drug-eluting bead transarterial chemoembolization (DEB-TACE), has the ability of administering embolic microspheres loaded with cytotoxic drugs into the hepatic artery in a more sustained and controlled fashion. This enables the maintenance of high concentrations of the drug at the tumor location for a period lasting from several days to one month.[24]

Use of small drug-eluting microspheres (DEM-TACE) and balloon occlusion catheters (B-TACE) represent newer approaches to chemoembolization, albeit with less comparative data in HCC treatment at this stage.[23,39-41]

TACE induce local tumor necrosis by the occlusion of feeding arteries, leading secondarily to the release of tumor antigens, which activate the immune response. [42]Moreover, TACE can potentially modify the cytokine spectrum and the activation level of T cells.[43]

TACE stimulates the secretion interleukines (IL) as IL-1 and IL-10, and of Interferon-γ, with activation of T helper-17 and T helper-1 cells [8,86,87]. TACE also leads to a modulation of immunosuppressive factors such as T-regulatory cells, PD1/PDL1, and HIF-1α, potentially bringing immune tolerance. [35,44-46]

According to AASLD guidelines, TACE is a standard palliative treatment in the management of intermediate-stage HCC. Paul SB and colleagues evaluated the outcome of TACE therapy in patients with unresectable HCC in India. They concluded that TACE is safe and well tolerated. Postprocedure complications were mild with 13.6% showing postembolization syndrome, which included pain abdomen, fever, nausea, and vomiting.[47]

Agarwal et al evaluated the factors influencing the outcome of TACE in Indians and proposed that it is an effective and safe treatment in Child A and early Child B patients. Factors such as Child class B, larger tumor size, presence of portal vein thrombosis, metastasis, and high baseline alpha-fetoprotein levels have a negative effect on survival.[48]

ABLATION

Ablative techniques for HCC include radiofrequency ablation (RFA), microwave ablation (MWA), cryoablation (CA), irreversible

electroporation (IRE), laser-induced interstitial thermotherapy (LITT), and high-intensity focused ultrasound (HIFU). Thermal ablation aims to induce cell death through delivering a destructive local temperature change to the tumor tissue. Although multiple techniques have been described in the current clinical setting, microwave ablation (MWA) and radiofrequency ablation (RFA) are the most commonly used ablation techniques.[49]

Both RFA and MWA techniques generate high temperatures in target locations to coagulate tissue, they do so based on different mechanisms;

RFA relies on electrical current, whereas MWA utilizes electromagnetic energy. Additionally, MWA possesses some advantages over RFA, including faster ablation time, the ability to deliver higher temperatures and the production of larger and more uniform ablation zones. [50,51]

This is aided by the fact that MWA is less susceptible to the “heat sink” effect, which arises when tumors are located in the proximity of large blood vessels and are incompletely ablated due to heat loss. [52]

In addition, there is no risk of burning, meaning it can be used in patients with metallic structures such as pacemakers who cannot be exposed to the electrical current of RFA.[53]

MICROWAVE ABLATION (MWA)

Surgical resection or orthotopic liver transplantation is the mainstay of treatment for very early and early-stage (BCLC 0, A) HCC patients.[54] However, most patients are disqualified from surgical intervention due to significant comorbidities, portal hypertension, poor hepatic function, cardiovascular comorbidities, inability to tolerate general anesthesia, or lesion location.[55,56]

As such, ablation offers a potentially curative option for these patients with early HCC with some studies demonstrating equivalent survival outcomes to resection even with poorer baseline liver function. [57,58,59]

Ablation with curative intent is an effective alternative to resection, particularly for tumors smaller than 3 cm.[60]

For tumors 3–5 cm in diameter, the combination of TACE and ablation demonstrate good outcomes albeit not curative. [61-64]

Caution must be exercised when lesions are close to major vessels, biliary structures, diaphragm, and other intra-abdominal organs. Hydrodissection, or artificial ascites, wherein 5% dextrose in water (D5W) fluid is injected between the tumor area and adjacent extrahepatic organ to prevent transmission of thermal energy, helps to separate the tumor and protects against unintentional organ injury. [65-67]

MWA can also be considered in advanced stage patients (BCLC C) for downstaging as a bridge to transplantation and in intermediate stage patients (BCLC B) when combined with TACE. [68]

Microwave Ablation MWA is a minimally invasive thermal ablation technique used in the treatment of HCC. It involves the application of high frequency electromagnetic waves ≥900 MHz using needle-like microwave antennae that are inserted into the tumor site under ultrasound, CT or MRI guidance to induce tumor damage. MWA is preferably conducted percutaneously (P-MWA), which is the most minimally invasive of possible approaches, and can be repeated if tumor recurrence occurs. However, when tumors are not accessible percutaneously, MWA can also be performed laparoscopically (L-MWA), thoracoscopically or via laparotomy.[24,69]

MWA uses an electrode to deliver thermal energy-induced cellular destruction. MWA may be suitable for larger tumors than RFA is indicated for and highly perfused regions.[70]

Rapid directional current changes in the microwave electrode cause surrounding water dipoles to oscillate, resulting in heat generation leading to cellular coagulative necrosis.[71]

Moreover, MWA can target multiple tumor sites simultaneously, yields shorter time to threshold temperature, achieves larger ablation treatment zones, results in better delineated ablation zone borders, and is less prone to heat-sink effects from adjacent vascular structures.[60,72]

All ablative modalities utilize imaging guidance/monitoring during the procedures such as computed tomography (CT) or ultrasound (US), or a combination. New modalities such as contrast-enhanced US (CEUS)

have also been utilized as well as novel fused imaging technologies to predict treatment zones.[73,74]

Follow-up imaging with CT or MRI every 3–6 months for the first two years with serum alpha fetoprotein (AFP) monitoring is recommended by the NCCN.[75] Serious complications include injury to adjacent organs e.g., diaphragm, gastrointestinal tract, gallbladder.[76] A postablation syndrome (PAS) may occur with analogous clinical presentation and self-limiting nature.[77]

STAGING OF HEPATOCELLULAR CARCINOMA

Hepatocellular carcinoma (HCC) is different from other malignancies because the prognosis in HCC is not only dependent upon the tumor stage but also on the liver function impairment due to accompanying cirrhosis liver. Various other staging systems used in HCC include the European systems [French staging system, Barcelona Clinic Liver Cancer (BCLC) staging system and the cancer of the liver Italian program (CLIP)] and Asian systems [Okuda staging system, Japan integrated Staging (JIS), Tokyo score and Chinese University Prognostic Index (CUPI)]. Out of all the staging systems used in HCC, Barcelona Clinic Liver Cancer (BCLC) staging system is probably the best because it takes in to account the tumor status (defined by tumor size and number, presence of vascular invasion and extrahepatic spread), liver function (defined either by the Child-Pugh's class) and general health status of the patient (defined by the ECOG classification and the presence of symptoms).

Staging of hepatocellular carcinoma (HCC) is necessary for guiding prognostication, management, and research purposes that further aid in the improvement of existing clinical and epidemiological health services. Though there are some new staging systems for HCC developed in different parts of the world, there is no globally accepted staging system that allows for comparison of current management protocols among heterogeneous populations.[78]

Patient selection for all locoregional therapies involves clinical and serologic evaluation of the patient including functional status, liver function tests, and clinical indices such as the CP grading (Child-

Pugh), ALBI (Albumin-Bilirubin), MELD (Model for End-stage Liver Disease), and ECOG (Eastern Cooperative Oncology Group) performance status scores for patient stratification and assessment. [79]Most patients with hepatocellular carcinoma (HCC) have associated chronic liver disease, the severity of which is currently assessed by the Child-Pugh (C-P) grade.[80]

TABLE 2: CHILD-PUGH CLASSIFICATION FOR SEVERITY OF CIRRHOSIS[80]

CLINICAL AND LAB PARAMETER	**POINTS**		
	1	**2**	**3**
Albumin (g/dL)	>3.5	2.8-3.5	<2.8
Bilirubin (mg/dL)	<2	2-3	>3
Ascites	Absent	Mild moderate	Severe
Encephalopathy	None	Mild moderate	Severe
Prothrombin time/International Normalised Ratio (PT/INR)	<1.7	1.8-2.3	>2.3
CLASS A = 5-6 points: least severe disease **CLASS B = 7-9 points: moderately severe disease** **CLASS C = 10-15 points most severe disease**			

THE ALBI GRADE

The ALBI grade offers a simple, evidence-based, objective, and discriminatory method of assessing liver function in HCC that has been extensively tested in an international setting. The model, the Albumin-Bilirubin (ALBI) grade, performed at least as well as the C-P grade in all geographic regions. The majority of patients with HCC had C-P grade A disease at presentation, and within this C-P grade, ALBI revealed two classes with clearly different prognoses. Its utility in patients with chronic liver disease alone supported the contention that the ALBI grade was indeed an index of liver (dys)function. This new model eliminates the need for subjective variables such as ascites and encephalopathy, a requirement in the conventional C-P grade.[79,81.82]

MODEL FOR END-STAGE LIVER DISEASE (MELD) SCORE

The Model for End-Stage Liver Disease (MELD) consists of serum bilirubin and creatinine levels, International Normalized Ratio (INR) for prothrombin time, and etiology of liver disease. The MELD scale is a reliable measure of mortality risk in patients with end-stage liver disease and suitable for use as a disease severity index to determine organ allocation priorities.[83,84] Value ranges from 6 to 40.

BARCELONA CLINIC LIVER CANCER (BCLC) STAGING SYSTEM

The BCLC staging system matches liver dysfunction, tumor burden, and performance status to a recommended therapy.

Specifically, the BCLC utilizes Child-Pugh score and Eastern Cooperative Oncology Group (ECOG) status in addition to indicators of tumor burden. BCLC stratifies patients into five stages, categorized from stage 0 for “very early detection” to stage D for the most advanced disease cases.[85-91]

Although in most studies, the approach to the treatment of patients of HCC is designated into various staging systems, the most commonly used of which being the Barcelona Clinic Liver Cancer (BCLC) staging system. [85]

The value of the BCLC is in its ability to stratify the survival of patients with HCC among the substrata of 0, A, B, C, and D, and therefore it can be easily applied directly to patient care. The BCLC may offer the most prognostic information because it includes an assessment of tumor burden, liver function, and patient Performance status (PS) and thereby has been endorsed by the societies that specialized in liver disease.[92]

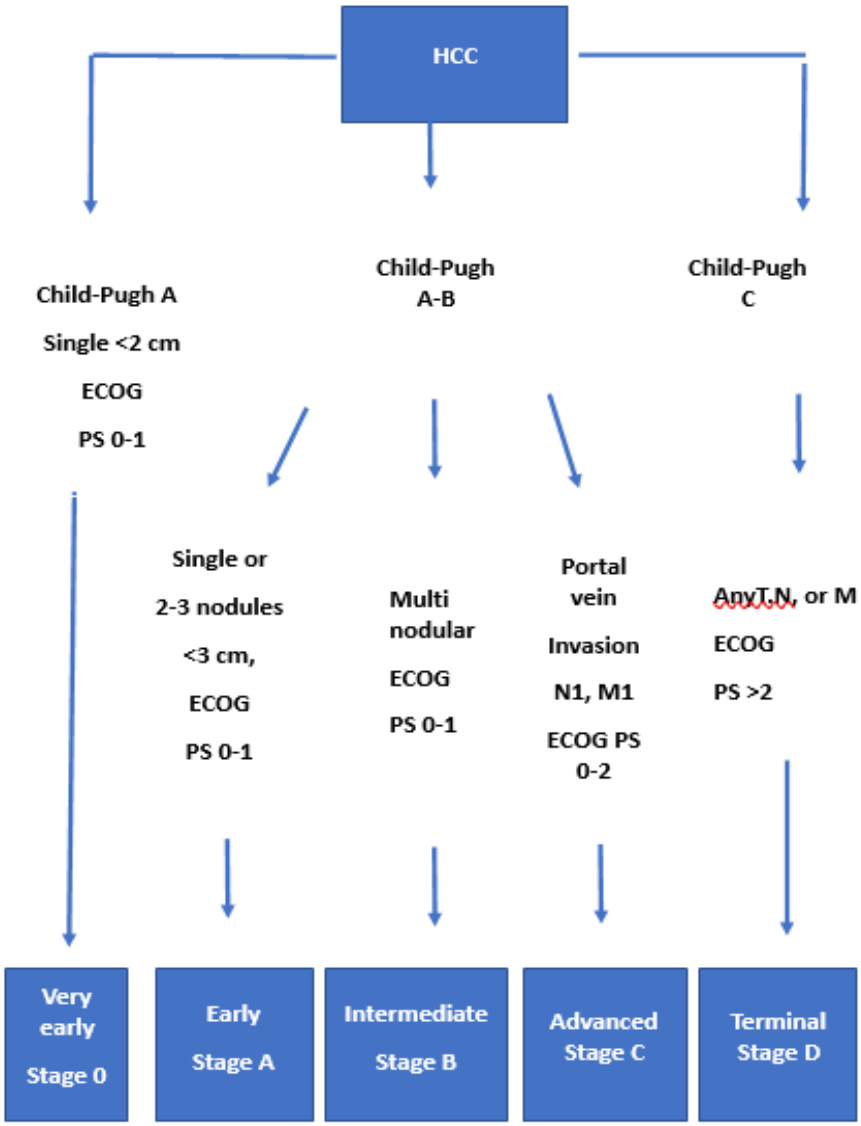
The prognostic ability of the BCLC has been validated in European, American, and Asian populations. The value of the BCLC is in its ability to stratify the survival of patients with HCC among the substrata of 0, A, B, C, and D, and therefore it can be easily applied directly to patient care.[93-95]

The BCLC staging system are helpful in even advanced stage and not only help in prognostication but also in deciding the treatment

modalities; hence may be more applicable also to Indian patients with HCC.[96] The BCLC staging has been recently modified.[97]

Because the prognostic ability of this modification has not been prospectively validated, we have kept the previous iteration of the BCLC staging, that has been prospectively validated.

FIG 1: BARCELONA CLINIC LIVER CANCER (BCLC) STAGING SYSTEM [98]



BCLC HCC staging system. Abbreviations: N, Nodal metastasis; M, extrahepatic metastasis

TABLE 3: BARCELONA CLINIC LIVER CANCER (BCLC) STAGING SYSTEM [99]

	Performance status	Tumor burden	Liver function
Stage A (early)			
A1	0	Single, <5 cm	No PHT
A2	0	Single, <5 cm	PHT, normal bili
A3	0	Single, <5 cm	PHT, elevated bili
A4	0	Up to 3, <3 cm	Child–Pugh class A–B
Stage B (intermediate)	0	Large multinodular	Child–Pugh class A–B
Stage C (advanced)	1–2	Vascular invasion or extrahepatic disease	Child–Pugh class A–B
Stage D (end stage)	3–4	Any	Child–Pugh class C

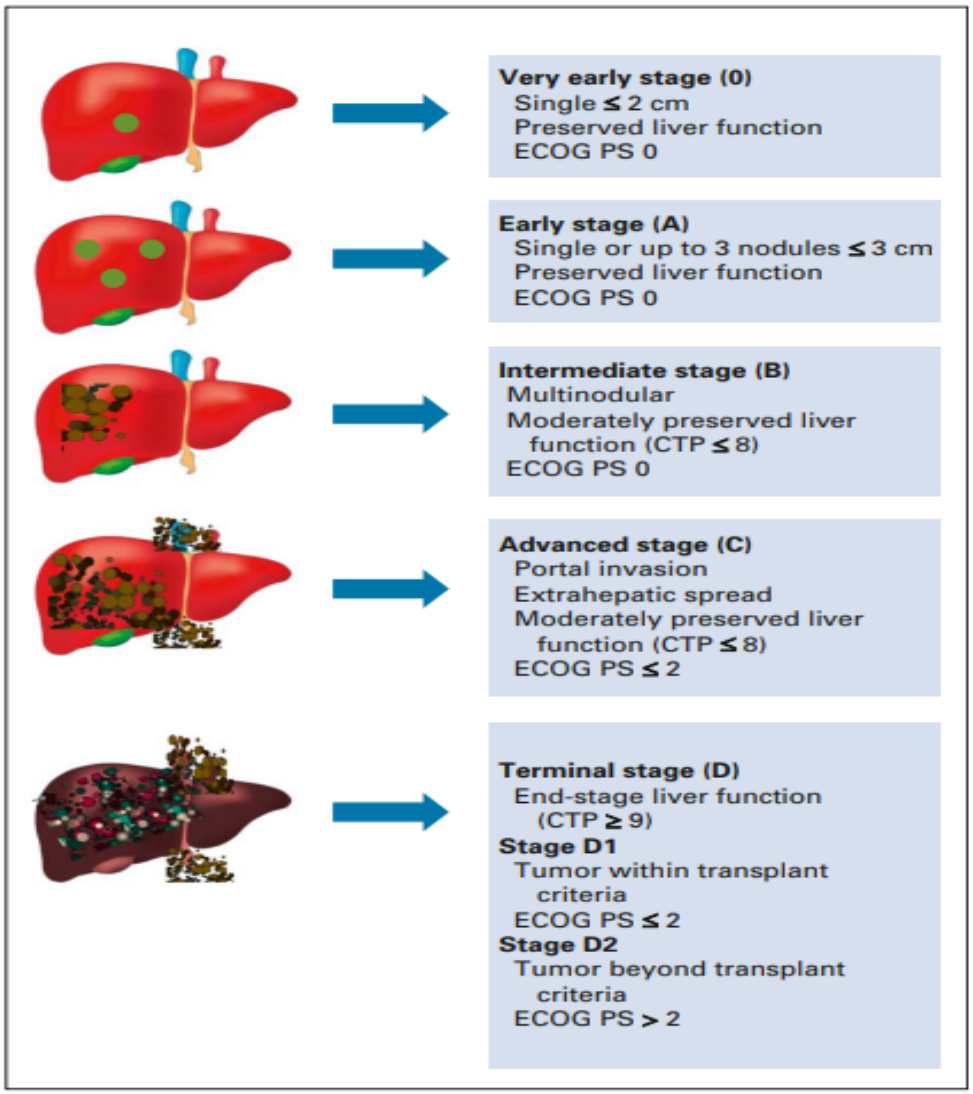
INASL, INDIAN NATIONAL ASSOCIATION FOR STUDY OF THE LIVER -MODIFIED BCLC STAGING OF HCC

The Barcelona Clinic Liver Cancer (BCLC) Staging System is a commonly used tool for guiding HCC treatment strategies both in clinical practice and in clinical trials. Nonetheless, limitations of this staging system include similar treatment recommendation for individuals with heterogeneous disease since they are classified as the same stage. Surgery is not recommended for patients with intermediate-stage HCC, and they are referred to palliative treatment as per BCLC staging. However, availability of new evidence suggests the need for BCLC criteria to be refined or possibly changed.[100-102] Indian National Association for Study of the Liver –introduced modified BCLC staging of HCC.[103]

FIG. INASL-modified BCLC staging of HCC. BCLC, Barcelona Clinic Liver Cancer; CTP, Child-Turcotte-Pugh; ECOG, Eastern Cooperative

Oncology Group; HCC, Hepatocellular Carcinoma; INASL, Indian National Association for Study of the Liver.

FIG 2: INDIAN NATIONAL ASSOCIATION FOR STUDY OF THE LIVER – (INASL)MODIFIED BCLC STAGING OF HCC[103]



GUIDELINES FOR HCC

Guidelines for HCC were recently developed according to the GRADE approach.[105]

These Guidelines were developed using clinically relevant questions, which were then answered by systematic reviews of the literature, focusing on surveillance, diagnosis, and treatment of HCC. However, some areas of HCC lacked sufficient data to perform systematic reviews, and hence the 2010 American Association for the Study of

Liver Diseases (AASLD) Guidelines,[99] are hereto used as the guidance for HCC in our study.

IMAGING MODALITY FOR LRT FOLLOW UP

Imaging plays a crucial role in the diagnosis of hepatocellular carcinoma (HCC) as well as in determining treatment efficacy, or complications, following therapy.

Several societies have developed guidelines to help standardize criteria for both the imaging diagnosis and assessment of treatment response in HCC, including Organ Procurement and Transplantation Network (OPTN)/United Network for Organ Sharing (UNOS), American Association for the Study of Liver Diseases (AASLD), Liver Imaging and Reporting Data System (LI-RADS), and the European Association for the Study of the Liver (EASL).[106–109]

HCC is one of the few cancers where imaging appearance alone, without pathology, can be used to diagnose disease. Similarly, imaging is used to diagnose residual or recurrent disease following treatment with LRTs. Unfortunately, given the iatrogenically-induced changes that can be associated with LRTs, determining treatment effect versus residual tumor can be difficult.[22]

The AASLD recommends multiphase CT or multiphase MRI for the diagnostic evaluation of patients with HCC because of similar performance characteristics.[110]

A recent meta-analysis reported sensitivity of MRI with extracelluar or hepatobiliary agents for HCC diagnosis exceeds that of CT.[111]

In comparison analyses among CT, contrast-enhanced ultrasound (US) and MRI was found to be the most sensitive and specific modality in determining the presence or absence of residual tumor following TACE.[112]

MRI has both better contrast delineation between the HCC and liver as well as more sequences to dissect out a HCC from the underlying liver leading to MRI’s higher sensitivity than CT with nearly 100% specificity.[113]

TECHNIQUE OF MULTIPHASE ENHANCEMENT MRI

A basic MRI exam consists of standard sequences which include T2-weighted imaging both with and without fat suppression, T1-weighted in- and opposed-phase sequences, diffusion-weighted imaging (DWI), and unenhanced followed by dynamic contrast-enhanced (DCE) 3D gradient-recalled echo fat-suppressed imaging using either gadolinium-based extracellular or hepatobiliary agents.

DCE images typically consist of an arterial phase (AP), portal venous phase (PVP) (65–85 seconds from the beginning of injection), and a delayed phase (DP) (3–5 minutes from beginning of injection). The optimal AP is the “late arterial phase” (LAP) defined as contrast visualized in the hepatic artery, portal vein, but not yet in the hepatic veins. This allows time not only for the contrast agent to be delivered to the arterial fed tumor but also for the contrast agent to proceed into the tumor interstitium, allowing the tumor to enhance relative to the surrounding liver parenchyma. A HCC will typically have hyperenhancement during the LAP with “washout” (the tumor’s lower signal intensity compared with the adjacent liver) during the PVP and/or DP to meet major criteria for HCC imaging diagnosis, either at initial diagnosis or as evidence of residual/recurrence post LRT.[22,114-115]

TECHNIQUE OF MULTIPHASE ENHANCEMENT CT

While CT has been shown to be less effective in HCC detection and characterization than MRI, CT does have qualities that can make it an exam of choice. CT takes less patient cooperation, is less affected by large volume ascites, is potentially safer in patients with renal failure, is more readily available, and is cheaper than MRI. The optimal multidetector, multiphasic CT consists of four separate phases through the liver: noncontrast, LAP, PVP and DP, with timing that mirrors that of MRI. While MRI has other criteria available to help in HCC display, CT has mainly the various phases of contrast enhancement. The AP hyper enhancement and washout of the PVP and/or DP will be used to assess for HCC in both pre- or posttreatment.[22]

POST TACE TREATMENT CHANGES

Lipiodol stains the treatment area/tumor for months following cTACE, while the contrast given with DEB-TACE and TAE typically washes out after a few hours.[116,117]

After cTACE, patients are typically imaged with a noncontrast CT within 24 hours to evaluate lipiodol distribution. The presence of lipiodol being taken up in the entire tumor is associated with complete necrosis.[118]

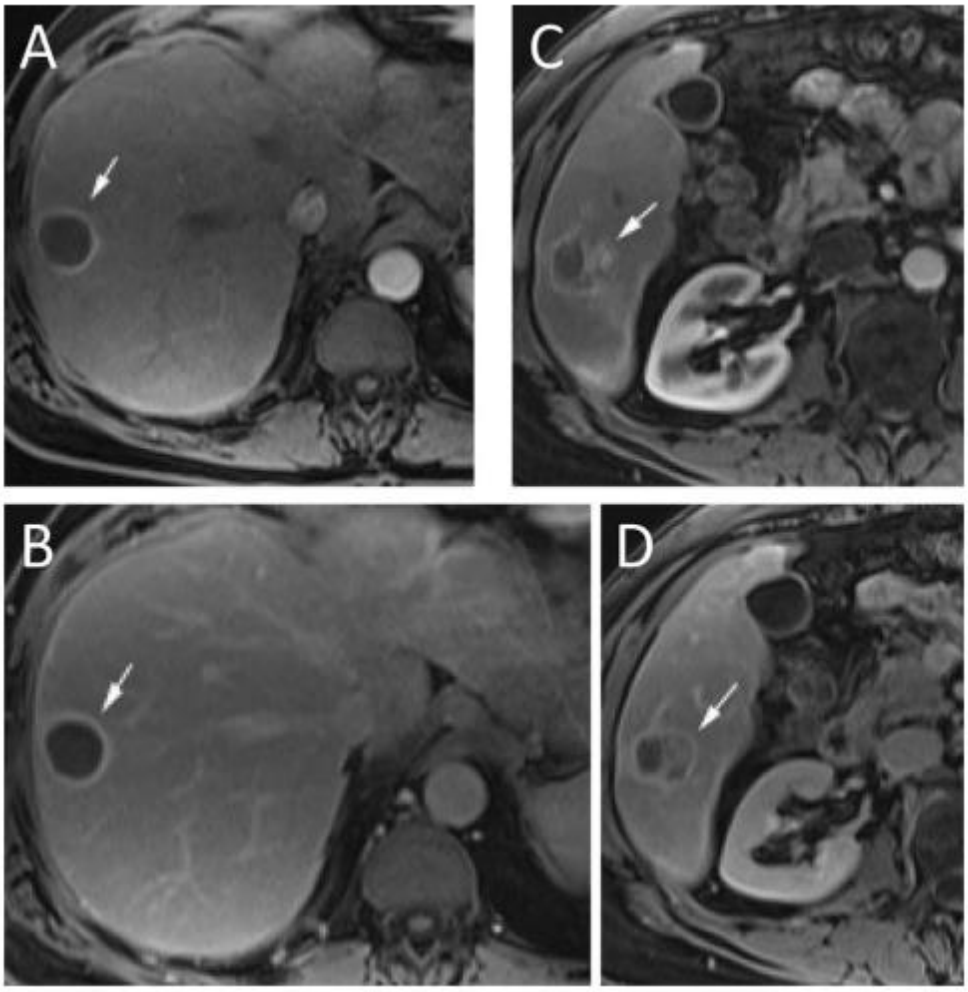
If the tumor does not show lipiodol coverage, the patient can be scheduled for a repeat TACE without having to wait for delayed follow-up imaging. If only a portion of the lesion is stained, it is not likely that the lesion will achieve complete response, and alternative-feeding arteries should be sought.[119]It is common for HCC lesions to require more than one TACE to achieve maximal response.[120]

Similar to ablation, post-TACE results are best evaluated on contrast-enhanced CT or MRI. As with ablation, lack of enhancement is a surrogate for tumor death, and has been found to correlate well with pathologic necrosis.[119]

Following TACE, as with ablation, it is not uncommon to see a thin rim of enhancement around the treated lesion. If this rim is < 5 mm in width and shows persistent enhancement, not washout, on portal venous phase imaging, it most often does not signify recurrence (Fig. A and B).[116]

Residual tumor (in another patient) is primarily demarcated by nodular, usually >5 mm, areas that demonstrate arterial enhancement and subsequent washout. Recurrences are most commonly at the edge of the treatment area (Fig. C and D).[121]

PICTURE 1: POST-TACE TREATMENT. NO RESIDUAL TUMOR (A AND B) AND RESIDUAL DISEASE PRESENT (C AND D).[22]



Picture 1 Post-TACE treatment. No residual tumor (A and B) and residual disease present (C and D). (A) Arterial phase imaging, 1 month after TACE demonstrates a thin (5 mm) area of enhancement (arrow). (D) This nodular area of enhancement (arrow) demonstrates washout on portal venous phase imaging. These findings are consistent with recurrent HCC

IMAGING AFTER ABLATION: POST ABLATION TREATMENT CHANGES

A common post-ablation finding is a hypervascular rim surrounding the ablation zone that can remain for several months. This hypervascular rim is initially secondary to hyperemia and then inflammation resulting from the ablation process.[122] The imaging manifestation of this hypervascular rim is seen during arterial enhancement. One study

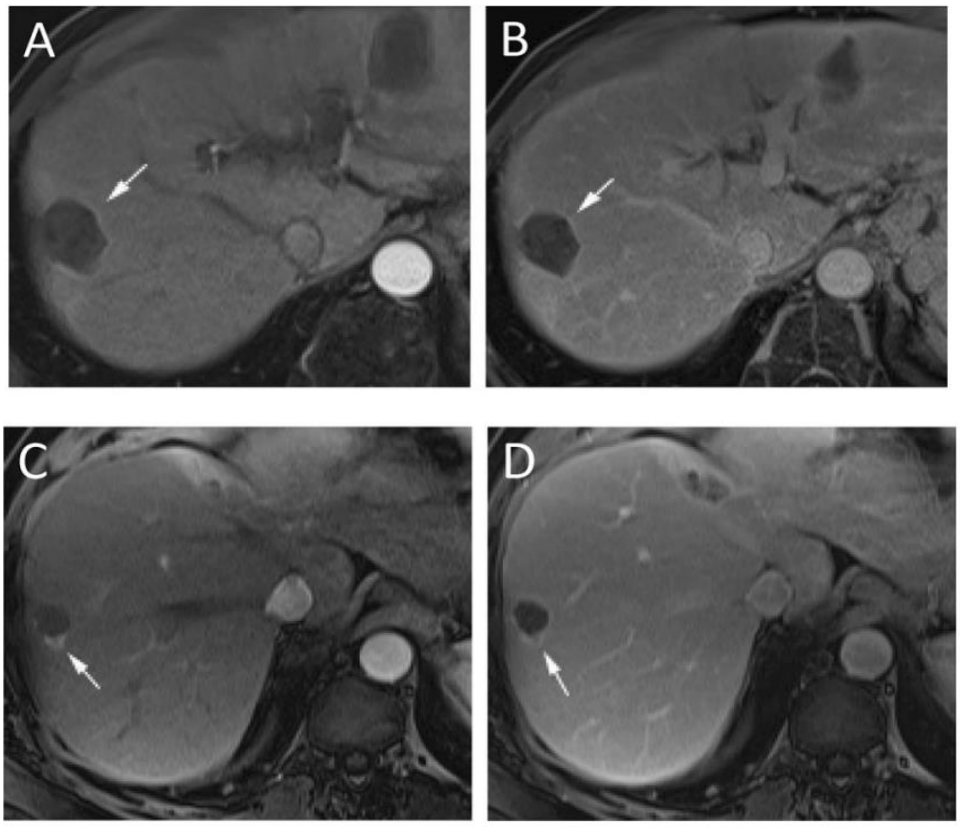
demonstrated this rim in 89% of cases at 1 month, 56% at 1–3 months, and 22% at 3–6 months imaging.[123]

This expected posttreatment rim enhancement should be < 5 mm, which may continue into the PVP (Fig. A and B). Conversely, residual/recurrent disease along the periphery is typically associated with >5 mm area of AP enhancement and/ or washout on PVP/DP imaging (Fig. C and D).[116,124]

Picture 2: post- MWA treatment changes.

(A) Arterial phase imaging, 1 month after MWA demonstrates a thin (<5 mm) rim (arrow) of enhancement without nodularity. (B) The thin rim of enhancement (arrow) persists on portal venous phase imaging. These findings are consistent with expected post treatment changes and not recurrence. In another patient, residual/recurrent disease along the periphery is typically associated with >5 mm area of AP enhancement and/ or washout on PVP/DP imaging (Fig. C and D). [116,124]

PICTURE 2: POST MWA TREATMENT CHANGES. NO RESIDUAL TUMOR (A AND B) AND RESIDUAL DISEASE PRESENT (C AND D). [22]



LIVER IMAGING REPORTING AND DATA SYSTEM (LI-RADS)

Liver Imaging Reporting and Data System (LI-RADS), on the other hand, has its own treatment response algorithm (TRA) for the evaluation of tumor viability after LRT. [125]

The LI-RADS classification system should be applied only to patients with cirrhosis or chronic hepatitis B infection or with current or prior HCC. Is should not be applied to patients under the age of 18 years. The LI-RADS, in addition to the arterial phase hyperenhancement (APHE) used in mRECIST, also evaluates the washout appearance (hereafter, washout) and “enhancement similar to pretreatment” to assess tumor viability.[126]

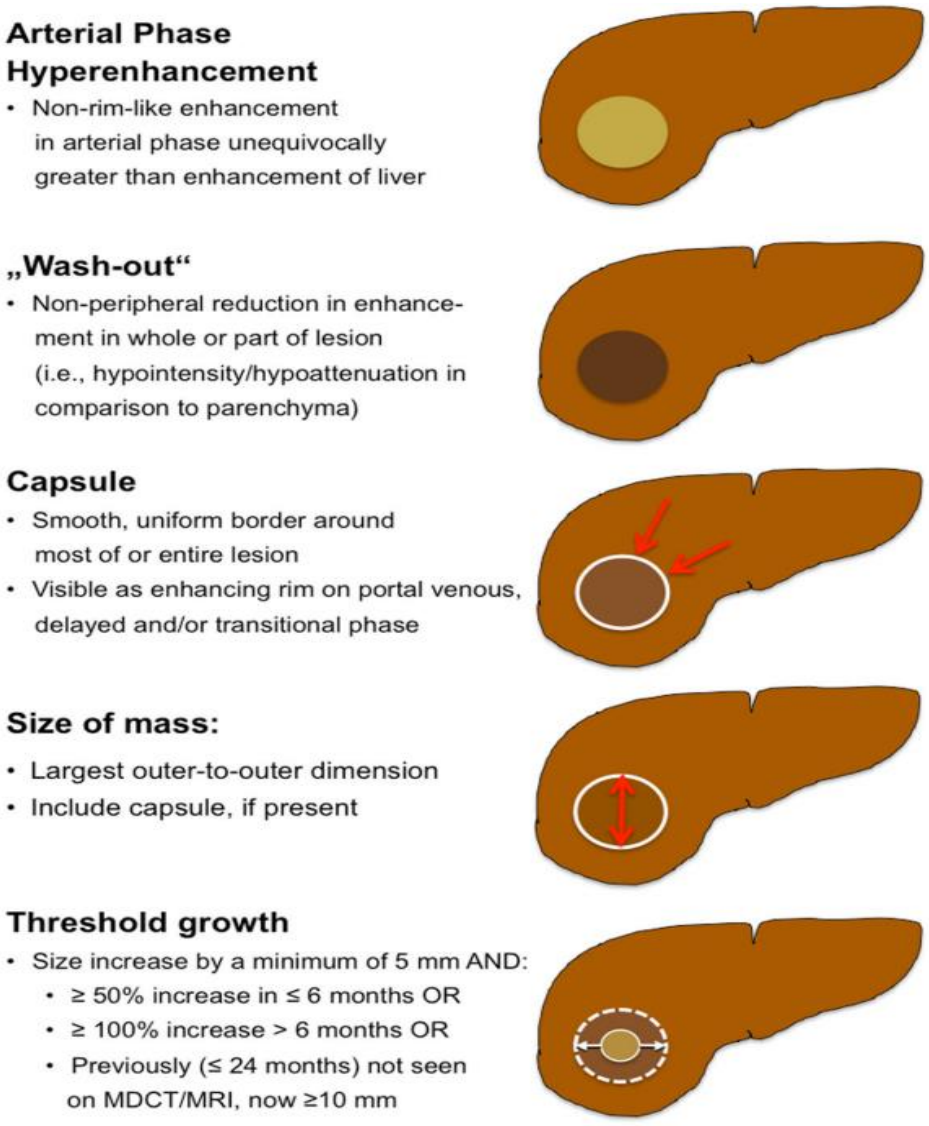
The major criteria are applied for evaluation of liver nodules with size (< 10 mm, 10–19 mm, ≥ 20 mm); arterial phase hyper-enhancement or arterial phase hypo- or iso-enhancement, washout appearance (signal intensity/attenuation loss to hypointensity/hypoattenuation in the venous and/or delayed phase), presence of an enhancing “capsule” around the lesion and threshold growth (minimum increase of 5 mm and ≥ 50% diameter increase in ≤6 months or ≥ 100% increase in ≤1 year). These major features are used to assign an observation to categories LI-RADS 3–5 (Figs. 3). Each observation is assigned a LIRADS category according to the major features observed.[127]

TABLE 4: LI - RADS CATEGORY CODES

RATING NODULES ACCORDING TO LI-RADS [127]

LI-RADS Category codes		
LR-1	Definitely benign	Cysts, hemangioma
LR-2	Probably benign	Atypical haemangiomas and focal parenchymal abnormalities likely attributable to underlying cirrhosis
LR-3	Indicates a low probability of HCC.	
LR-4	Indicates probable HCC	
LR-5	Indicates definite HCC.	
LR-M	Is assigned to observations with features highly suggestive or even diagnostic of malignancy, but not specific for HCC.	
LR-TIV	Vascular-invasive disease or tumor in vein	
LR-TR	Treated HCC mass	
LRTR-VIABLE	Ca in situ	
LR-NC	Non categorizable	
LR TR-NV	Non-viable, no Ca	
LR-Equivocal	Not sure	

FIG 3: LI-RADS MAJOR IMAGING FEATURES[127]


Arterial Phase Hyperenhancement
• Non-rim-like enhancement in arterial phase unequivocally greater than enhancement of liver
„Wash-out“
• Non-peripheral reduction in enhancement in whole or part of lesion (i.e., hypointensity/hypoattenuation in comparison to parenchyma)
Capsule
• Smooth, uniform border around most of or entire lesion
• Visible as enhancing rim on portal venous, delayed and/or transitional phase
Size of mass:
• Largest outer-to-outer dimension
• Include capsule, if present
Threshold growth
• Size increase by a minimum of 5 mm AND:
• ≥ 50% increase in ≤ 6 months OR
• ≥ 100% increase > 6 months OR
• Previously (≤ 24 months) not seen on MDCT/MRI, now ≥10 mm

CONTRAST-ENHANCED ULTRA-SOUND (CEUS)

Another method that may be used for HCC diagnosis in expert centers is contrast-enhanced ultrasound (CEUS). A recent meta-analysis of CEUS for HCC showed a pooled sensitivity of 85% [128,129] and a specificity of 91% (95% CI, 90-92).[130]

However, the meta-analysis noted significant issues, including small cohort sizes, potential selection bias for patients with adequate quality USs, lack of generalizability with differences of studies in Asia versus Western countries, etc.

TREATMENT PROTOCOL AND STRATEGY FOR HCC

A key component to ensuring good outcomes in patients with HCC is maintenance of good liver function. There is a need to better refine patient selection for locoregional therapies for achieving better outcomes. This may involve validating subclassifications of intermediate HCC and/or developing better predictive biomarkers for therapy.

LOCOREGIONAL THERAPIES (LRTS)AND SYSTEMIC THERAPIES

There have been significant advances in HCC treatment over the past 10 years with improvements in both technology and patient selection. Available therapeutic options can be divided into curative and noncurative interventions. Curative therapies include surgical resection, orthotopic liver transplant (LT), and ablative techniques such as thermal ablation.

Each of these approaches offers the chance of long-term response and improved survival. Noncurative therapies, which attempt to prolong survival by slowing tumor progression, include trans-arterial chemoembolization (TACE), transarterial radioembolization (TARE), stereotactic body radiation therapy (SBRT), and systemic chemotherapy.

Locoregional therapies (LRTs) are novel procedures evolved now and play a leading part in the management of 50–60% of HCCs. LRT is defined as imaging-guided liver tumour-directed procedures; with the aid of ultrasound guidance, an antitumoral device, drug, or chemical is introduced directly into the tumor and causes tumor death. Improved outcomes have been achieved with these innovative techniques which are employed for diverse applications ranging from curative-intent for small-localized tumors, to downstaging or bridging to resection and transplantation for early and intermediate disease, and locoregional control and palliation for advanced disease.[35,131]

Interventional oncology has joined surgical, radiation, and medical oncology as a pillar of cancer care. Minimally invasive treatment options have expanded with improvements in image guidance and novel low-profile devices that allow for targeted cancer therapy without

the morbidity of open surgery or the diffuse toxicity of systemic chemotherapy and radiation therapy.[24]

In addition to its role in the diagnosis of HCC, preprocedural imaging is paramount for evaluation of the vascular anatomy, access site patency, and ensuring patency of the portal vein.[132]

In addition, with the advent of more effective systemic therapies, the decision to stop locoregional therapy and switch to systemic therapy is evolving and must be individualized to the patient's situation. Studies need to be carried out to address the optimal treatment algorithm for transitioning from locoregional to systemic therapy and vice versa. It remains to be seen whether combination approaches with systemic and locoregional therapies will result in further paradigm shifts.[133]

FIGURE 4a: DIAGRAM SUMMARIZING LOCOREGIONAL THERAPIES[24]

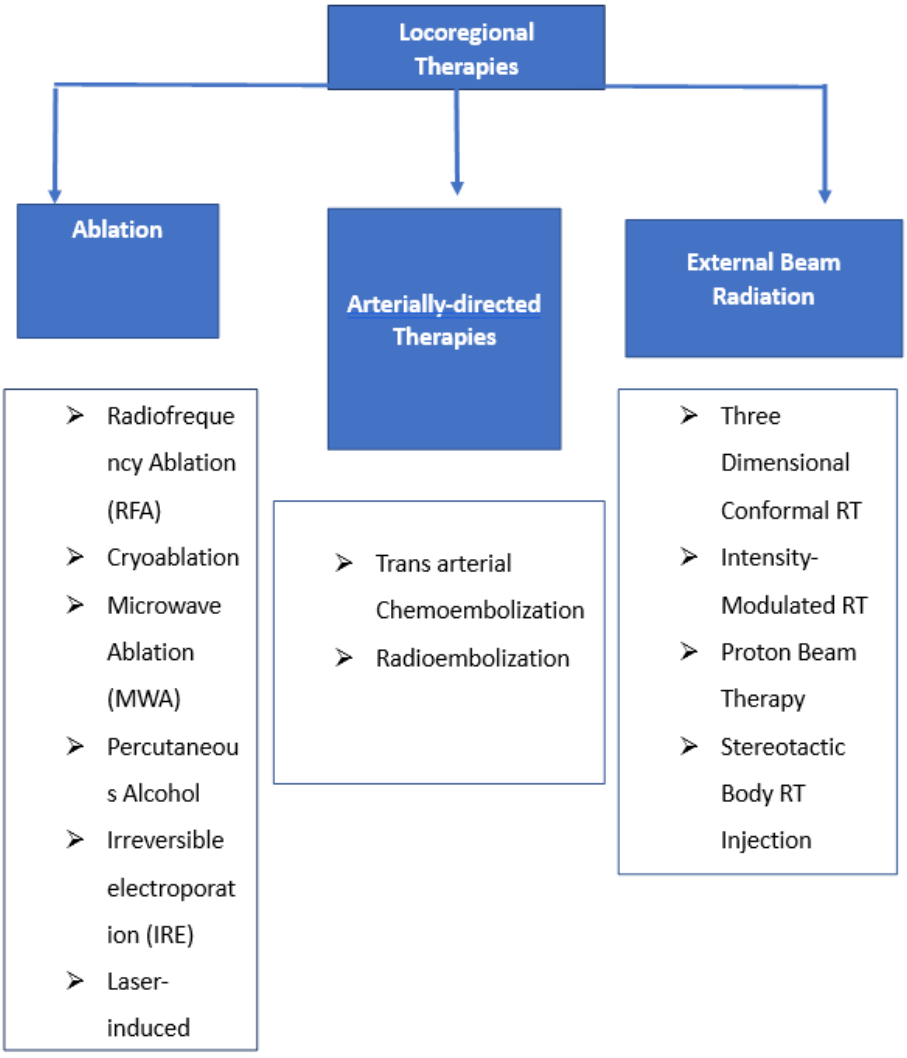


FIGURE 4b: DIAGRAM SUMMARIZING SYSTEMIC THERAPIES[24]

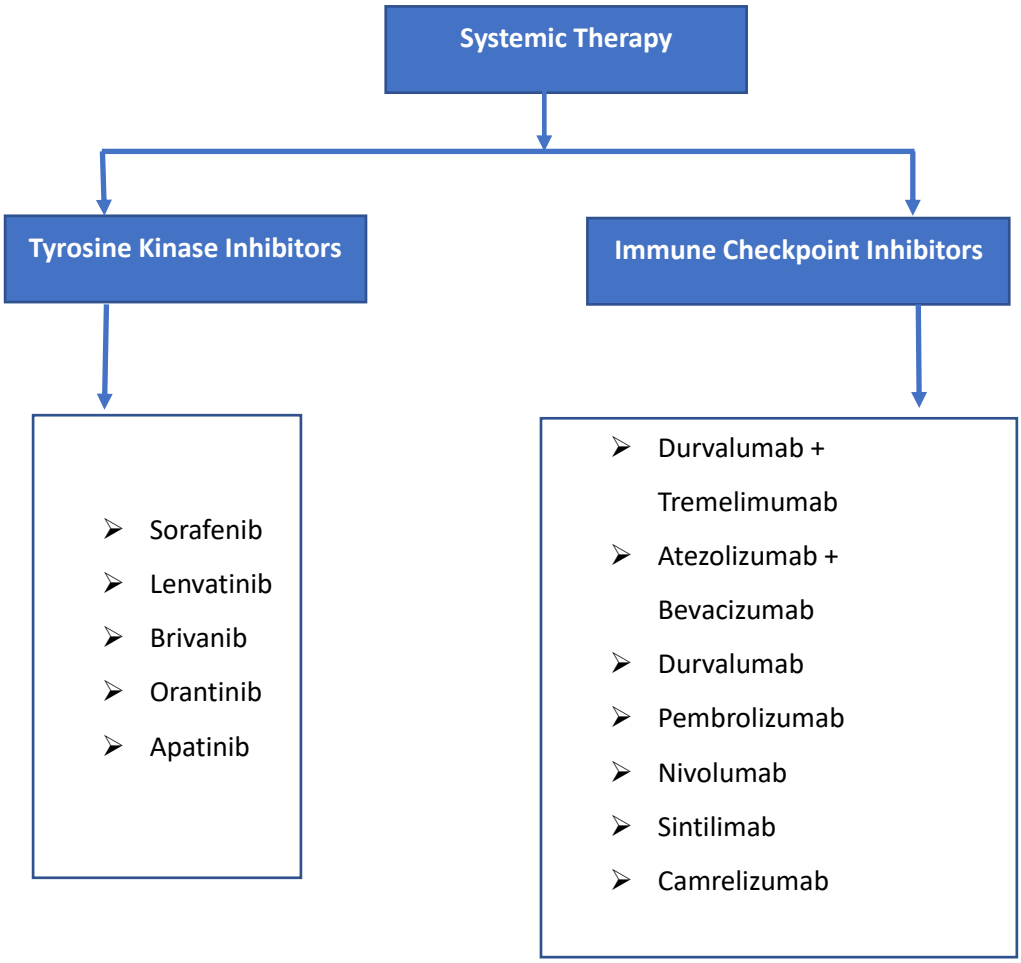
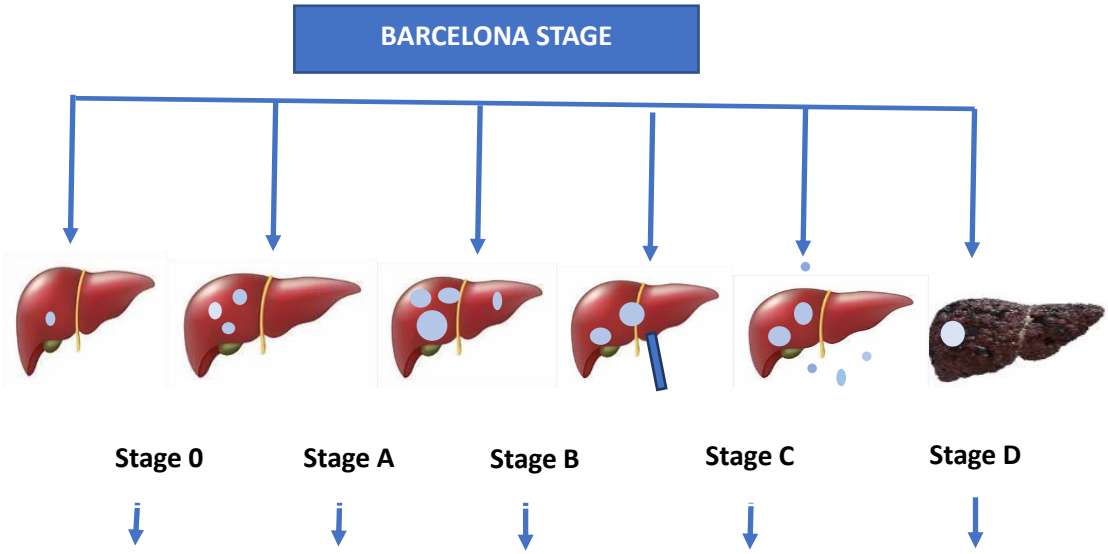


FIGURE 5: TREATMENT RECOMMENDATIONS ACCORDING TO BCLC STAGE.[98]



Level of Evidence					
1	Resection		TACE	Sorafernib (IL) Lenvatinib (IL) Regorafemib (2L) Cabozantinib (2L)	
2	RFA MWA	Resection OLT RFA MWA TARE TACE SBRT	TARE Downsize OLT	Nivolumab (2L)	OLT BSC
3				TARE	

Abbreviations: MWA, microwave ablation; BSC, best supportive care; 1L, first-line therapy; 2L, second-line therapy

TABLE 5: TREATMENT RECOMMENDATIONS ACCORDING TO BCLC STAGES[29]

BCLC STAGES	DESCRIPTION	TREATMENT OPTIONS
Very early stage (BCLC 0)	➢ a solitary HCC ≤2 cm ➢ without vascular invasion or extrahepatic spread ➢ patient with preserved liver function and ➢ no cancer-related symptoms	liver transplantation (LT)
Early stage (BCLC-A)	➢ solitary HCC irrespective of size ➢ or as a multifocal HCC up to 3 nodules (none of them >3 cm) ➢ without macrovascular invasion, extrahepatic spread or cancer-related symptoms (PS-0).	➢ Resection and RF ablation offer the same survival benefit for HCC ≤2 cm [38,39] ➢ MW achieves more extensive tumour necrosis than RF and is potentially the best option for those patients with HCC ≤4 cm [96–98]. ➢ Larger tumours may still benefit from resection as size alone should not be considered a limiting factor for surgical resection ➢ Radiation lobectomy by TARE
Intermediate stage (BCLC-B)	➢ This is defined as multifocal HCC ➢ with preserved liver function, ➢ no cancer-related symptoms (PS 0) ➢ no vascular invasion or extrahepatic spread. As well known, the magnitude of tumour burden may be quite heterogeneous in this stage, and prognosis is also influenced by AFP concentration	LT, TACE TACE (liver function has to be well preserved), or systemic therapy

First subgroup within BCLC-B	➢ includes patients with well-defined HCC nodules ➢ Elevated AFP values predict a higher risk of HCC recurrence A 1,000 ng/dl cut-off value is currently applied as an exclusion criterion.	Candidates for LT if they meet the 'Extended Liver Transplant criteria
Second subgroup within BCLC-B	➢ comprises patients without the option of LT but who have preserved portal flow and defined tumour burden, ➢ suggesting the feasibility of selective access to feeding tumour arteries	Candidates for TACE. OR Systemic therapy should be considered.
Third subgroup within BCLC-B	➢ patients with diffuse, infiltrative, extensive HCC liver involvement.	Systemic therapy
Advanced stage (BCLC-C)	➢ Has vascular invasion or extrahepatic spread ➢ who are still relatively fit, as reflected by a PS ≤2 at staging work-up ➢ who have preserved liver function.	Systemic therapy
End-stage (BCLC-D)	➢ (PS >2) and/or impaired liver function	Palliative care

OUT COME ASSESSMENT: RESPONSE CLASSIFICATION SYSTEMS

Response classification systems have been developed to standardize terminology, assist in research standardization, and improve interdisciplinary dialogue. Initial classification systems included the Response Evaluation Criteria in Solid tumors (RECIST) and World Health Organization (WHO) guidelines that focused on the overall size

of the lesion based upon the sum of diameters, using one (RECIST) or two axial dimensions (WHO).[134–136]

The most widely used tool for measuring tumoral response to treatment in HCC is the 2010 modified Response Evaluation Criteria in Solid Tumors (mRECIST).[137,138]

These systems, which were designed primarily for cytotoxic, systemic therapy, fell short in evaluating the response following LRT. The WHO and RECIST criteria revolve around measuring the size of the lesion without accounting for the cellular makeup or viability of that lesion. Because LRTs induce necrosis, through various methods, WHO and RECIST criteria inadequately report the change in tumor viability. Using these criteria can lead to apparent “tumor progression”, as the post-LRT treatment zone is frequently larger than the initial tumor dimensions. Because of these limitations two new response classification systems were developed, the modified Response Evaluation Criteria in Solid Tumors (mRECIST) and EASL guidelines.[138, 139]

These criteria use contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI) to assess response by using **arterial enhancement as a marker** f**or residual, viable tumor** and **the lack of enhancement as a marker for necrosis**. Enhancement is critical in post-LRT imaging because the appearance of necrosis is variable and unreliable on noncontrast enhanced imaging.[140,141]

These systems measure the maximal diameter of the residual tumor (that is, the arterial enhancing portion) in one (mRECIST) or two (EASL) axial dimensions and classify the effect to treatment as complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD). The definition of each response category by classification system can be found in Table 6

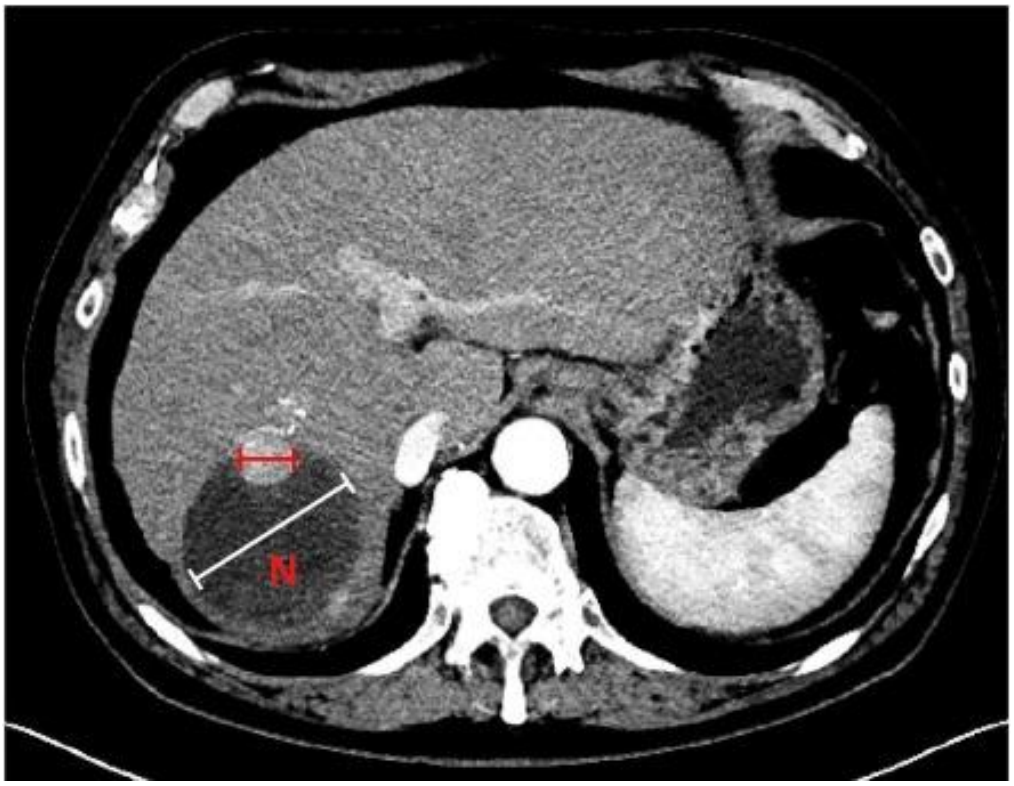
mRECIST(modified RECIST) proposed in 2010, is the standard tool for measuring radiological endpoints at early and intermediate stages of HCC, and evidence is growing regarding its relevance in advanced HCC[138]

TABLE 6: mRECIST - MODIFIED RECIST [RESPONSE EVALUATION CRITERIA IN SOLID TUMORS][138]

Response	mRECIST: Unidirectional Ax measurement	EASL: Bidirectional Ax measurement
Complete response (CR)	No residual area of disease	No residual area of disease
Partial response(PR)	30% decrease in size	50% decrease in size
Progressive disease (PD)	20% increase in size or new lesion	25% increase in size or new lesion
Stable disease (SD)	**Neither PR nor PD criteria met**	**Neither PR nor PD**

Abbreviations: Ax, axial; EASL, European association for the study of the liver; mRECIST, modified response evaluation criteria in solid tumors

PICTURE 3: MEASUREMENT OF THE LONGEST TUMOUR DIAMETER IN A TARGET HEPATIC LESION; MRECIST VS. STANDARD RECIST [142]



Arterial-phase CT scan obtained after systemic targeted therapy. According to standard RECIST, the overall longest diameter of the tumour is captured (white arrow), regardless of the presence of a large area of intratumoural treatment-induced necrosis (“N”). In contrast, mRECIST measurement (red arrow) only includes the longest diameter of the viable portion of the tumour, as recognized by contrast enhancement. mRECIST, modified RECIST.

PICTURE 4: APPLICATION OF mRECIST ASSESSMENT FOR HEPATOCELLULAR CARCINOMA (HCC). [142]

Target tumor response measurements on arterial-phase computed tomography (CT) scans. (A) Measurement of longest overall tumor diameter according to conventional RECIST, and (B) measurement of longest viable tumor diameter according to mRECIST for HCC.

AIMS AND OBJECTIVES

The study was planned and conducted to evaluate the outcome of locoregional interventional therapies (LRT) offered to patients with Hepatocellular carcinoma (HCC) registered in the Department of Radiodiagnosis in Dayanand Medical College and Hospital, Ludhiana, N. India. The study was conducted prospectively and retrospectively over a period of 3 years. The clinical outcome in these patients in relation to response to LRT was assessed using the modified Response Evaluation Criteria in Solid tumors (mRECIST) criteria.

REVIEW OF LITERATURE

EPIDEMIOLOGY

As per the GLOBOCAN 2018 report, liver cancer is the third leading cause of cancer-related deaths worldwide and contributed to 781,631 (8.2%) deaths in 2018. [143]Liver cancer was responsible for 14,000 cancer deaths in India in 2010, with an age-standardized cancer mortality rate of 6.8 (5.4-8.1) per 100,000 cases.[144]According to Population-Based Cancer Registry from 2012 to 2014, Sikkim and Arunachal Pradesh have the highest incidence of liver cancer among all cancers in the country.[145]

Most Asian countries are in intermediate or high incidence zones of HCC. In India, the mean incidence of HCC in four population-based registries is 2.77% for males and 1.38% for females. The prevalence of HCC in India varies from 0.2% to 1.6%.[146]

AGE

Median age of presentation of HCC for Indian patients is noted to be 40-70 years.[146,147]

Incidence of HCC in India occurs at two peaks, one at a young age 45 to 55years. and another above 60 years. The two peaks occur because of acquiring hepatitis B either in utero or in childhood, or exposure in adulthood.[148] All HCCs occurring in the age group below 14 years are hepatitis B positive.[149]

GENDER

HCC is more common in men than in women, male to female ratio Is approximately 4:1. The available data suggest that age-adjusted incidence rates of HCC range from 1 to 7.5 per 100,000 population, 0.7 to 7.5 among men, and 0.2 to 2.2 in women.[146,150]

BASIC DIAGNOSIS

70% of the total HCC patient population is cirrhotic. Hepatic decompensation is seen in 50%, with 5% of patients presenting with encephalopathy.[148]

ETIOLOGY

Chronic hepatitis B virus (HBV) infection was found to be responsible for 44% of all HCC cases worldwide, followed by hepatitis C virus (HCV) infection (21%)[151]HBV and HCV infection, cirrhosis of the liver, combined with alcohol was the most common risk factor for HCC in India (63.9%).[152,153]

Obesity, diabetes mellitus (DM), and nonalcoholic fatty liver disease (NAFLD) are other important risk factors.[7] NAFLD has become a major risk factor for chronic liver disease, cirrhosis, and HCC in India.[154-156] NAFLD seems to have surpassed hepatitis B as the most common cause for HCC. In a 3-year observational study in a tertiary care center in India, most common etiology of HCC was found to be NAFLD/cryptogenic in 51% of the patients, followed by 17.4% for hepatitis B and 5.8% for hepatitis C.[157]About 3%-15% of obese patients with NASH (Non-alcoholic steatohepatitis) develop cirrhosis, whereas about 4%-27% of patients with NASH with cirrhosis acquire to HCC. Therefore, diagnosis of HCC in its early stages, even among patients with noncirrhotic NAFLD, is essential. [156]

SURVEILLANCE

HCC has an estimated 5-year survival rate of only 18%, which is partly due to the fact that only 30%- 40% of patients are discovered early and thus suitable for curative treatments such as liver resection (LR), ablation, or liver transplantation (LT). Most of them are diagnosed at a later stage with widespread liver disease, vascular invasion, and metastasis.[146,157]

HCC surveillance helps to identify early tumors that are amenable to treatment. Global associations, including the American Association for the Study of Liver Diseases (AASLD), European Association for the Study of the Liver (EASL), Asian Pacific Association for the Study of the Liver (APASL), and Indian National Association for Study of the Liver (INASL), advocate a 6-monthly abdominal ultrasonogram for HCC surveillance.[7-9,110]The INASL 2019 Consensus recommends the following patients to be subjected to surveillance for HCC: (1) Child's A and B cirrhotic patients of any etiology; (2) Child's C cirrhotic patients

of any etiology who are listed for LT; (3) patients with chronic hepatitis B (CHB) who have increased risk for HCC according to risk scores such as Chinese university (CU-HCC) or platelets, age, gender-hepatitis B; and (4) chronic HCV with advanced fibrosis.

Surveillance ha to be based on ultrasound examination. The recommended screening interval is 6 months. Diagnosis of HCC should be based on imaging techniques and/or biopsy. The 2005 diagnostic algorithm has been validated and the diagnostic accuracy of a single dynamic technique showing intense arterial uptake followed by ‘‘washout’’ of contrast in the venous-delayed phases has been demonstrated.[127]

INVESTIGATIONS- AFP

AFP is considered positive if its value is >20 ng/mL and negative if lower. Based on receiver operating curve Hepatology, Vol. 68, No. 2, 2018 MARRERO ET AL. 729 analysis, this threshold provides a sensitivity of around 60% and a specificity of around 90%. [98] Saini et al[149] evaluated the clinical and biochemical parameters in hepatocellular carcinoma and reported that the normal value of AFP in India is around 10 to 20 ng/mL. a level greater than 400 ng/mL which is accepted by European Association for Study of Liver (EASL) as diagnostic, is seen only in 46% of patients approximately 20% of patients have normal values.

Improved detection of hepatocellular carcinoma by using a longitudinal alpha-fetoprotein screening was recommended by Tayob et al 2016.[158]

In the first subgroup within BCLC-B which includes patients with well-defined HCC nodules, elevated AFP values predict a higher risk of HCC recurrence, and a 1,000 ng/dl cut-off value is currently applied as an exclusion criterion for LT. [157]

ANTIVIRAL PROPHYLAXIS

Because of widespread availability of antiviral medication, the long-term clinical results in patients with CHB have improved considerably in recent decades.[158]

Antiviral therapy in patients with BCLC-D may improve liver function, expanding the therapeutic window for tumor specific medicines.[8]

Immunomodulators (conventional interferon alpha and pegylated interferon alpha) and nucleoside/nucleotide analog (lamivudine, adefovir, entecavir, telbivudine, and tenofovir) have shown short term efficacy in the treatment of CHB. Long-term studies using lamivudine and adefovir reveal a consistent decrease in development of HCC in both cirrhotic and noncirrhotic patients.[159]

Another class of antivirals currently in clinical trials for treatment of HCV-related HCC is direct-acting antivirals, which have improved the cure rate to 90%. Yet, because of high costs and underdiagnosis in certain subpopulations, access to these drugs is limited.[160]

LIVER CANCER STAGING SYSTEM

Staging of hepatocellular carcinoma (HCC) is necessary for guiding prognostication, management, and research purposes that further aid in the improvement of existing clinical and epidemiological health services.

Out of all the staging systems used in HCC, Barcelona Clinic Liver Cancer (BCLC) staging system is probably the best because it takes in to account the tumor status (defined by tumor size and number, presence of vascular invasion and extrahepatic spread), liver function (defined either by the Child-Pugh's class) and general health status of the patient (defined by the ECOG classification and the presence of symptoms). BCLC staging system[98] was the tool used in our study for selection patients as well as management with respect to TACE or MWA procedures.

LIVER IMAGING REPORTING AND DATA SYSTEM (LI-RADS),

Liver Imaging Reporting and Data System (LI-RADS), on the other hand, has its own treatment response algorithm (TRA) for the evaluation of tumor viability after LRT.[125] Each observation is assigned a LIRADS category according to the major features observed.[127]LI-RADS Category codes is summarized as follows; LR-1- Definitely benign, LR-2- Probably benign, LR-3- Indicates a low probability of HCC, LR-4- Indicates probable HCC, **LR-5-Indicates definite HCC**., LR-M-Is assigned to observations with features highly suggestive or even diagnostic of malignancy, but not specific for HCC., LR-TIV-

Vascular-invasive disease or tumor in vein , LR-TR-Treated HCC mass, **LRTR-VIABLE- Ca in situ**

LR-NC-Non categorizable, **LR TR-NV -Non-viable, no Cancer**, LR-Equivocal- Not sure. The LI-RADS, in addition to the arterial phase hyperenhancement (APHE) used in mRECIST, also evaluates the washout appearance (hereafter, washout) and “enhancement similar to pretreatment” to assess tumor viability.[126,127]

In our study LI-RADS was used for selection of patients before treatment and evaluating the treatment response.

(mRECIST) CRITERIA

The most widely used tool for measuring tumoral response to treatment in HCC is the 2010 modified Response Evaluation Criteria in Solid Tumors(mRECIST).[137,138]

These systems measure the maximal diameter of the residual tumor (that is, the arterial enhancing portion) in one (mRECIST) or two (EASL) axial dimensions and classify the effect to treatment as complete response- No residual area of disease(CR), partial response - 30% decrease in size(PR), stable disease-20% increase in size or new lesion (SD), or progressive disease- Neither PR nor PD criteria met (PD).

OUTCOME AND SURVIVAL

Burrelet al.[161] investigated the survival of patients with hepatocellular carcinoma treated by transarterialchemoembolisation (TACE) using drug eluting beads. demonstrated a median survival up to 47.7 months after TACE for BCLC B patients.[161]

Golfieri et al[162] in a single-center retrospective review of 271 patients with 635 HCCs treated with TACE analysed a subgroup of lesions that were 2.1–5 cm and found that the radiologic response rates, according to mRECIST criteria, after one session of cTACE were complete response (CR) in 64% (134/211 nodules) and PR in 36% (77/211 nodules). In our study, CR after one session of TACE was 15%, which is considerably lower.

Lee et al.[163] evaluated 337 patients with HCCs between 3 and 5 cm, 150 of whom underwent TACE and found that overall survival (OS) at

1, 3, and 5 years for this cohort of 150 patients was 88.7%, 56.7%, and 36.7%, respectively. Survival in our TACE group was 46%, 6 month post treatment.

Yin et al[164] investigated the long-term outcome and prognostic factors for percutaneous thermal ablation technique in medium and large hepatocellular carcinoma and found out that in the patients with 3- to 5-cm HCCs, 80.7% (71/88) had a CR after an initial intervention and 95.4% (84/88) achieved CR if secondary interventions were allowed. In our study, survival outcome in MWA patients was 93% which was comparable to the above findings.

MATERIALS AND METHODS

SOURCE OF DATA

The study is a retrospective observation from the Department of Radiodiagnosis in Dayanand Medical College and Hospital, Ludhiana, a Tertiary teaching institute in North India, Punjab. The study extended over a period of 3 years. We studied patients with HCC who were initially deemed not to be candidates for liver transplantation, surgical resection, or underwent any previous LRTs.

A total of 28 patients were included. All met the diagnostic criteria for HCC. After thorough discussion of their case with their consulting physician and interventional radiologist regarding their treatment options, patients had undergone locoregional interventional therapy for treatment of HCC.

In the present study, data of patients treated for HCC, given that the patient data included is complete and reliable. The study was done with the approval of the ethics committee.

We collected clinical details, possible etiological factors, complete blood count, liver function tests, renal function tests, viral markers and details of viral infection and treatment (for Hepatitis B and C) from medical records section. Radiological imaging studies for LRTs were documented; before treatment and three follow up details 6 weeks, 3 months post treatment.

METHOD OF COLLECTION OF DATA

INCLUSION CRITERIA

HCC patients in whom LRT was performed in accordance with BCLC staging and treatment strategy.

EXCLUSION CRITERIA

1. Evidence of exrahepatic metastasis.
2. Serum bilirubin >2 mg/dl
3. Presence of portal vein or inferior vena cava thrombosis, or biliary duct invasion.
4. Severe liver cirrhosis with Child-Pough class C.

5. Severe coagulation disorders (prothrombin concentration less than 60% and platelet count less than 70,000/mm3).
6. Presence of significant ascites.
7. Encephalopathy
8. Those having severe co-morbidities (coronary artery disease, chronic renal disease, respiratory disease)
9. Insufficient data

DURATION OF STUDY**:** 3 years retrospective and prospective study

TREATMENT STRATEGIES:

The Barcelona Clinic Liver cancer (BCLC) staging and treatment strategy the most internationally accepted staging and treatment algorithms for HCC. The same is used in our study for reference to decide a treatment plan for our HCC patients,

According BCLC strategy the indications of MWA is as follows

a. BCLC Stage 0; Very Early stage

i. Single nodule <2cm in size

ii. Child-Pugh A with Performance status 0

with/without raised Portal venous pressure and associated disease.

b. BCLC Stage A; Early stage

i. Single or ≤3 nodules ≤ 3 cm in size.

ii. Child-Pugh A-B with Performance status 0 with/without raised Portal venous pressure and Associated disease

According BCLC strategy the indication of TACE is as follows:

a. BCLC stage B; Intermediate stage.

i. Large multinodular

ii. Child-Pugh A-B with Performance Status 0

Contraindications for these therapies would be:

a. BCLC stage C; advanced stage
   i. Portal invasion
   ii. Extrahepatic spread
   iii. Child-Pugh A-B with Performance status 1-2

a. BCLC stage C; Terminal stage

Child Pugh C with Performance status 3-4

In patients of HCC with established cirrhosis severity of cirrhosis will be assessed using the Child-Pugh score and MELD score

The Interventional therapies for HCC included in present study in Dayanand medial college and hospital are:

a. Microwave thermal ablation (MWA)

b. Transarterial chemoembolization (TACE) using DEB-TACE or HepaSphere-TACE

STUDY DESIGN

The study is designed to be prospective and retrospective utilizing clinical, hematological, biochemical details as well as documented radiological imaging studies of LRT patients; at the time of intervention and 2 to 3 follow ups at 6 weeks, 3 months and 1 year post treatment.

OUTCOME

Outcomes will be assessed according to mRECIST criteria, the following definitions will be applied for tumor response to treatment:

A. Complete response: (CR)

The disappearance of any intratumoral arterial enhancement in all target lesions

B. Partial response: (PR)

At least a 30% decrease in the sum of diameters of viable (contrast enhancement in the arterial phase) target lesions, taking as the reference the baseline sum of the diameters of target lesions.

C. Progressive disease: (PD)

An increase of at least 20% in the sum of the diameters of viable (enhancing) target lesions, taking as the reference the smallest sum of the diameters of viable (enhancing) target lesions recorded since the treatment started.

D. Stable disease: (SD)

Any cases that do not qualify for either partial response or progressive disease.

STATISTICAL ANALYSIS

All statistical calculations will be done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows. Descriptive statistics were expressed as

percentages or mean and standard deviation. Continuous variables compared using paired T test or Non- parametric Wilcoxon signed rank test. Categorical variables were expressed as proportions and Chi square or Fisher's exact test as appropriate were used to define difference between the two groups. A two-tailed p value of less than 0.05 was considered statistically significant.

OBSERVATION AND RESULTS

This was a prospective study which included HCC patients who underwent Locoregional Therapy (LRT), registered under the Department of Radiotherapy, Dayanand Medical College and Hospital, Ludhiana a tertiary care institution in Punjab, India.

Results:

36 cases who met the inclusion for HCC were considered for the current study for a period of three years.

However only 28 cases were selected since 8 patients did not have complete case records.

13 (46.4%) patients underwent Trans-arterial Chemoembolisation TACE, and 15(53.6%) had Microwave Thermal Ablation, MWA.

Age: Age of patients ranged from 46 to 84 years with the mean age of 60.7± 8.6 years. The maximum number of patients in the study were in the age group 51 -70 years,11 (78.6%). The mean ages were comparable in both groups, 59.0 (9.2) vs.62.2 (8.8) in TACE and MWA groups respectively, p = 0.357

Gender: 22 (78.6%) were males and 6 (21.4%) females. M:F ratio was 3.6:1.There were 11(84.4%) and 11 (73.3%) males vs. 2 (15.4%) and 4 (26.7%) females in TACE and MWA groups respectively, with no statistically significant difference in gender distribution among patients, p = 0.468.

Method of first diagnosis: Majority of patients in both study group were identified by surveillance, 10 (76.9%) vs. 9 (60.0%) in TACE and MWA respectively, p = 0.339.

Basic Diagnosis: The predominant basic diagnosis in both groups was cirrhosis, 7 (53.8%) vs. 11 (73.3%0, in TACE and MWA groups respectively, with no statistically significant difference, p = 0.283.

Risk factors for cirrhosis: The most prevalent risk factor noticed among our patients was alcoholism 3 (23.1%) and 7 (46.7%) in TACE in MWA group respectively. The second prevalent risk factor was NASH, 5 (38.5%) VS. 4 (26.4%) in TACE and MWA group. 5 (38.5%) of TACE patients and 4 (26.7%) of MWA patients had HCV. Only 1(6.7%)

patient in MWA group had HBV infection. The observation was comparable in the two study groups, P >0.05.

Antiviral Treatment: All 5 (38.5%) patients in TACE group who had HCV, and all patients in MWA group with history of HCV or HBV 6 (40.0%) underwent antiviral treatment.

Prevalence of Ascites: Ascites was observed more on TACE group, 8 (61.5%) as compared to 7 (46.7%) in MWA group. The difference was not statistically significant p=0.431.

Encephalitis: Only one patient in TACE group had this complication, which resolved before he was considered for treatment.

Biochemistry: No statistical difference was observed in biochemical parameters between the two groups.

Hyperbilirubinemia was observed in 6 (46.2%) and 7 (46.7%) of TACE and MWA patients respectively, p= 0.724. There was no statistical difference was recorded among patients who had altered SGOT, SGPT and Alk. Pase levels. 3 (23.1%) and 2 (20.0%) patients had albumin less than 3 gm% in TACE and MWA groups, respectively. Serum AFP levels ranged from 8.7 to 366 ng/mL. One patient in TACE group had AFP value > 3000 ng/mL. AFP value > 44 was documented more in TACE patients, 5 (38.5%) vs. 2 (13.3%) MWA patients, respectively. But difference was not statistically significant.

Child-Pugh classification: Child-Pugh classification among LRT patient groups were comparable. There were 6 (46.2%) and 8 (53.3%) in Class A category and 7 (53.8%) vs. 7 (46.7%) were included in Class B category in TACE and MWA patients respectively. P= 0.477

BCLC staging: The Child-Pugh (CP) classification among LRT patient groups were comparable. 50% were included in Class A, 50.0 % in Class B.

MELD Score: A MELD score of more than 10 was observed in 8 (61.5%) and 9 (60.0%) in TACE and MWA groups respectively.

There were 4 (30.8%) vs.5 (33.3%) in stage A category in TACE and MWA groups respectively. Similarly, 9 (69.2%) vs. 9 (60.0%) were observed among TACE and MWA group respectively. In MWA group,

there were 1(6.7%) patient in stage 0. Differences were not statistically significant p = 0.076.

Number of lesions: Total number of lesions treated were 45, 23 lesions in TACE patients and 22 lesions in MWA patients. Maximum number of HCC lesions considered for treatment in one patient in our study group was 4. 19 patients had 1 lesion, 9 (69.2%) in TACE and 10 (66.7 %) in MWA patients. 2 lesions were observed in 3 (20.0%) of MWA patients. 3 lesions were documented in 4 patients, 2 (15.4%) and 2 (13.3%) in TACE and MWA groups, respectively. The maximum number of lesions treated in a single patient in MWA group was 3. 4 lesions were recorded in 2 (15.4%) patients who had TACE procedure. No statistical difference was there regarding number of lesions between the two study groups. P= 0.177.

The Couinaud segments: The Couinaud segments involved by the lesions were identified on the baseline CT/MRI and are tabulated. The most frequent couinaud segment involved was segment VI, with a total of 13 lesions, followed by segment VIII with 11 lesions and segment V with 6 lesions.

LI-RADS: Majority of lesions treated were diagnosed as either LI-RADS 5 or LI-RADS 4 in the CT/MRI triphasic imaging done prior to the procedure. Regarding lesion 1, all lesions 15 (100%) were LR-5 in MWA group vs 12 (92.3%) LR-5 and 1 (7.7%) LR-TIV lesions in TACE group.

At 6 weeks review after LRT, considering first lesion,there were 10 (76.9%) vs. 1 (6.7%) viable lesions in TACE and MWA respectively. Similarly, there were 2 (15.4%) vs.12 (80.0%) non-viable lesions in TACE MWA groups respectively, The difference was highly significant, **p=0.001**.

Tumor size: Tumor size in TACE group before treatment ranged from 1.3 x 1.1 cms to 12.1 x 10.14 cms, whereas tumor size in MWA group ranged from 0.8 cms x 0.8 cms to 5.5 x 5.0 cms. In one patient in TACE group lesion was described as large, multiple and nodulated nodules.

Tumor size > 5 cms was recorded in 9 (69.2%) in TACE group vs. (0%) in MWA group. Tumor size 3-5 cms were, 3 (23.1%) and 7 (46.7%) in TACE and MWA group respectively. Tumor size of ≤ 3 cms were observed in 1 (7.7%) and 8 (53.3%) in TACE and MWA groups, difference was highly significant, **p= 0.001**,

mRECIST, 6 weeks: The overall patient response to LRT at 6 weeks was analysed by mRECIST. One patient in MWA group died during procedure due to bleeding. Complete remission (CR) was observed in 11 (73.3%) in MWA group vs. 2 (15.4%) in TACE group. Partial remission (PR) was observed in 2 (15.4%) TACE group, none in MWA group. Stable disease (SD) was recorded in 4 (30.8%) and 1 (6.7%) patient in TACE and MWA group respectively. And Progressive disease (PD) was documented in 5 (38.5%) and 2 (13.3%) patients in TACE and MWA groups respectively. Differences were statistically significant. **p= 0.016**

3-month mRECIST follow up assessment: Complete tumor remission was observed more after MWA procedure than TACE, 60.0% vs. 23.1% respectively. Progressive disease and stable disease were seen more in TACE group, 46.2% and 30.8% respectively vs. 4 (27.7%) and 1 (6.7%) respectively among MWA subjects. But differences did not show statistical significance. p= 0.107

Survival: Survival out-come between the 2 LRT patient groups were obvious. Follow up after 6 months period documented 14(93.3%) vs. 6 (46.2%) live patients in MWA vs. TACE group respectively. Death happened in 5 (38.5%) patients in TACE, but only 1 (6.7%) in MWA group. 2 (15.4%) patients were lost to follow up in TACE group. The differences were statistically significant, **p = 0. 019**

Multivariate Cox regression Analysis:

Patients were classified in responders (complete and partial response) and non-responders (stable and progressive disease). And a multivariate analysis was done using the following predictors that can affect outcome.

Age <60, ≥60, Gender M/F, Detection by survillence or not, Risk factor alcohol/ not, Risk factor HCV/ not, AFP ≥ 400/ < 400 ng/ml,

Bilirubin>1.6 ng/ml/≤, Albumin< 3.3/ ≥3.3 g/, C-P grading A/ B, BCLC score A/ B, MELD Score <10/≥10, Tumor number 2/ > 2, tumor size 5/ >5 cms

None of the factors gave a significance to prove to be an independent risk factor to affect the treatment response.

TABLES AND FIGURES

DATA OF HCC PATIENTS WHO UNDERWENT LOCOREGIONAL THERAPY

1. **Gender:**

The demographic characteristics of patients were studied.

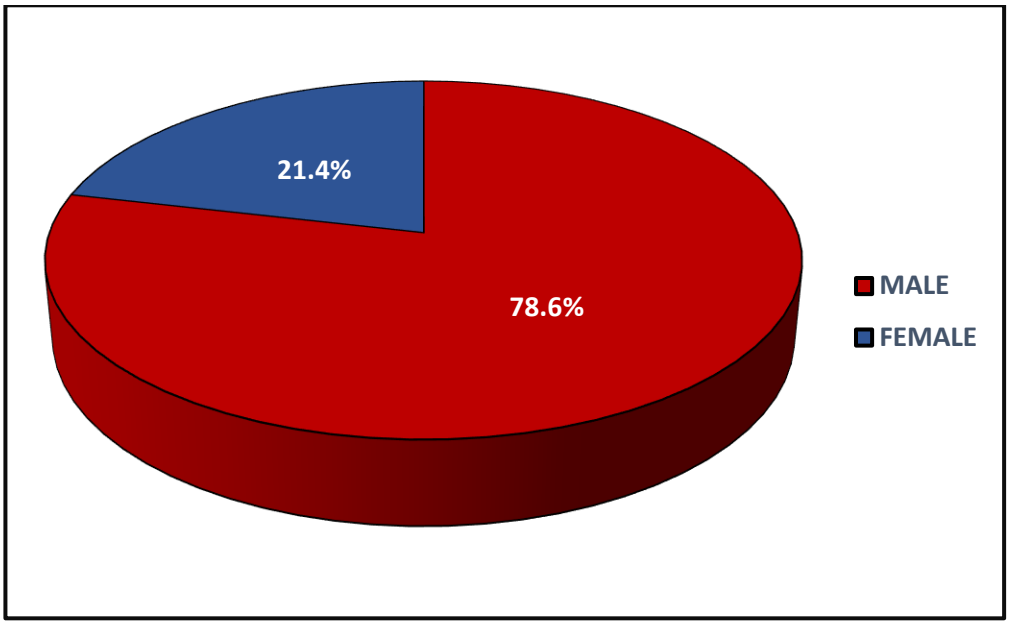
Among the 28 cases, 22 (78.6%) majority were males and 6 (21.4%) females. (Table-7, Fig-6). M:F ratio is 3.6:1.

There were 11(84.4%) males in TACE group vs. 11 (73.3%) among MWA group. There was no statistical difference between the groups regarding gender distribution, p= 0.468 (Table-7, Fig-6)

TABLE 7: GENDER DISTRIBUTION OF PATIENTS WITH HCC

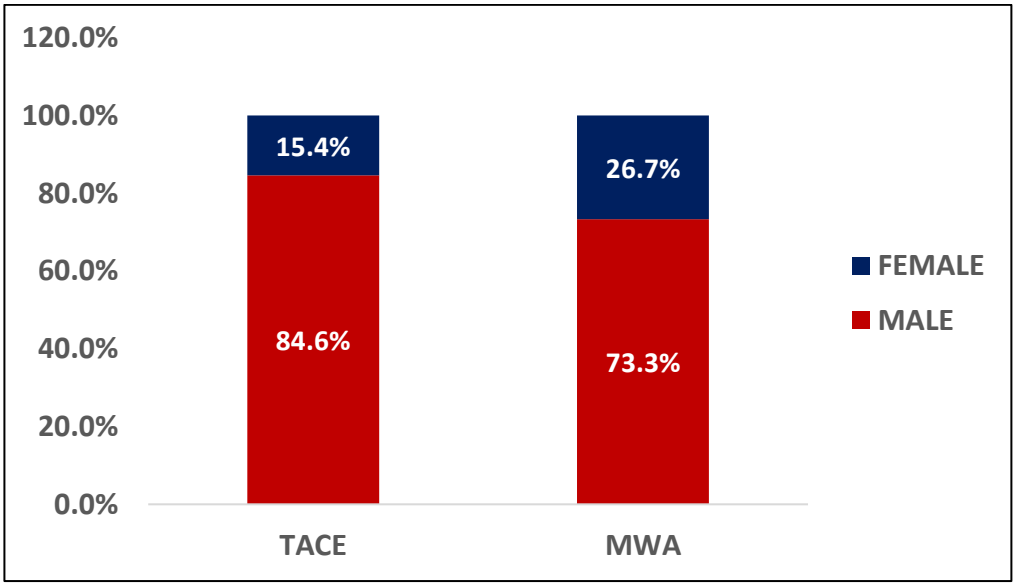
GENDER	TOTAL Number (%)	TACE Number (%)	MWA Number (%)	P value
Male	22 (78.6%)	11 (84.6%)	11 (73.3%)	0.468
Female	6 (21.4%)	2 (15.4%)	4 (26.7%)	
Total	28 (100%)	13 (100%)	15 (100%)	

FIG 6: GENDER DISTRIBUTION OF ALL PATIENTS WITH HCC



22 (78.6%) were males and 6 (21.4%) were females (Table-7, Fig-6). M:F ratio is 3.6:1.

FIG 7: GENDER DISTRIBUTION AMONG TACE AND MWA PATIENTS



Male predominance was evident in both TACE and MWA groups. There were 11(84.4%) and 11 (73.3%) males vs. 2 (15.4%) and 4 (26.7%) females in TACE and MWA groups respectively. There was no difference in gender distribution among patients, p = 0.468.

2. Age

The study group included patients with age ranging from 46 to 84 years with the mean age of 60.7± 8.6 years.

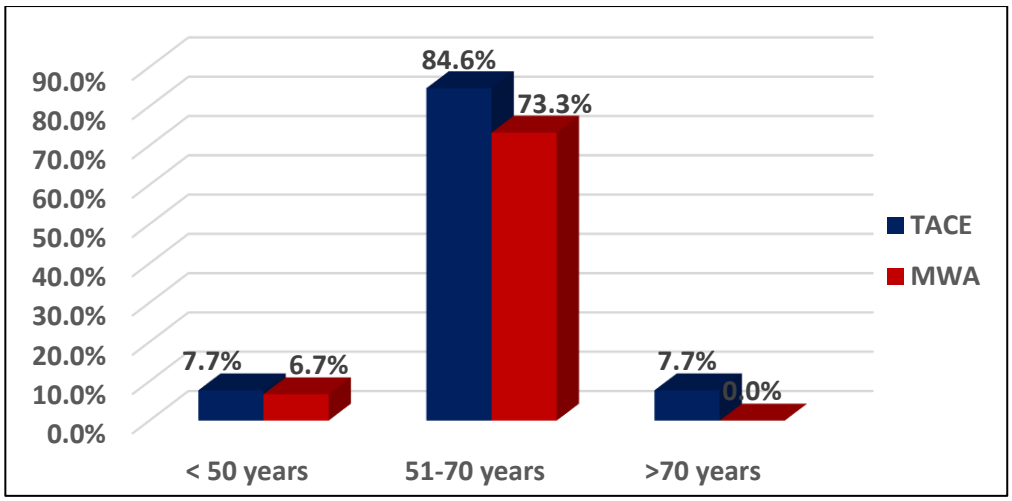
Majority of patients were among age group 51 to 70 years, 11 (84.6%) in TACE group vs. 11 (73.3%) in MWA group. There was no statistical difference between the two studied groups regarding age distribution, p = 0.164. (Table 8, Fig 8).

TABLE 8: AGE DISTRIBUTION OF HCC PATIENTS AT PRESENTATION

AGE (YEARS)	TACE Number (%)	MWA Number (%)	TOTAL Number (%)	P value
< 50	1 (7.7%)	1 (6.7%)		0.164
51-70	11 (84.6%)	11 (73.3%)	22 (78.6%)	
>70	1 (7.7%)	3 (20%)		
Mean (SD) Age (years)	59.0 (9.2)	62.2 (8.8)		0.357

The mean ages were comparable in both groups, 59.0 (9.2) vs.62.2 (8.8) in TACE and MWA groups respectively, p = 0.357 Table 8, Fig 8.

FIG- 8: AGE DISTRIBUTION OF PATIENTS WITH HCCAT PRESENTATION



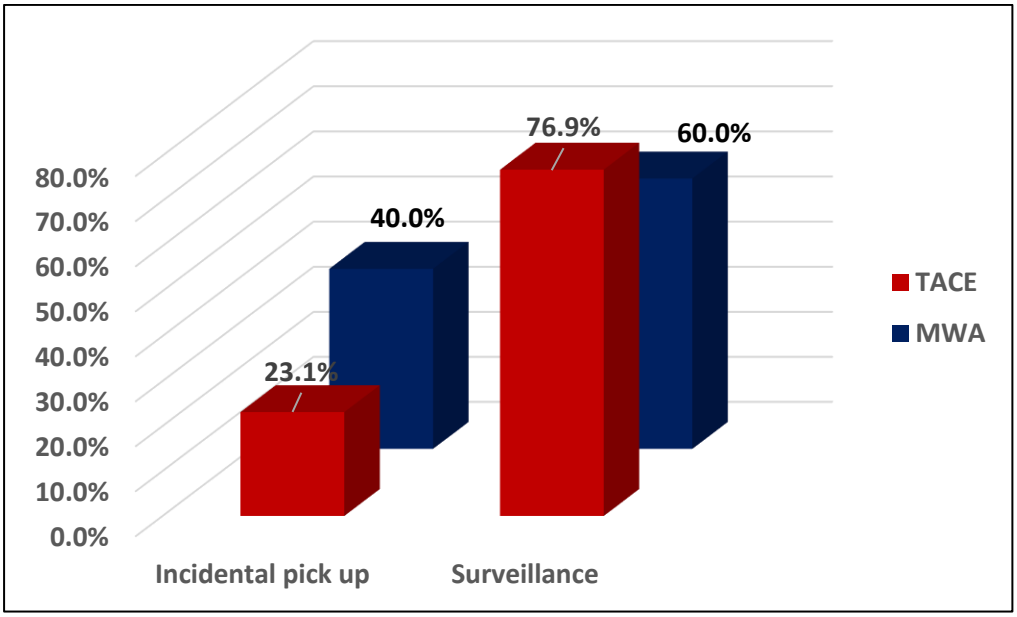
Majority of patients were in the range 51 to 70 years, 11 (84.6%) vs.11(73.3%) in TACE and MWA group respectively. Table 8, Fig 8.

2. Method of initial identification of HCC

TABLE 9: METHOD OF IDENTIFICATION OF HCC

PRESENTATION	TACE Number (%)	MWA Number (%)	TOTAL Number (%)	P value
Incidental pick up	3 (23.1%)	6 (40.0%)		0.339
Surveillance	10 (76.9%)	9 (60.0%)	19 (68.9%)	
Decompensated cirrhosis	0	0		

FIG 9: IDENTIFICATION OF HCC IN LRT PATIENTS



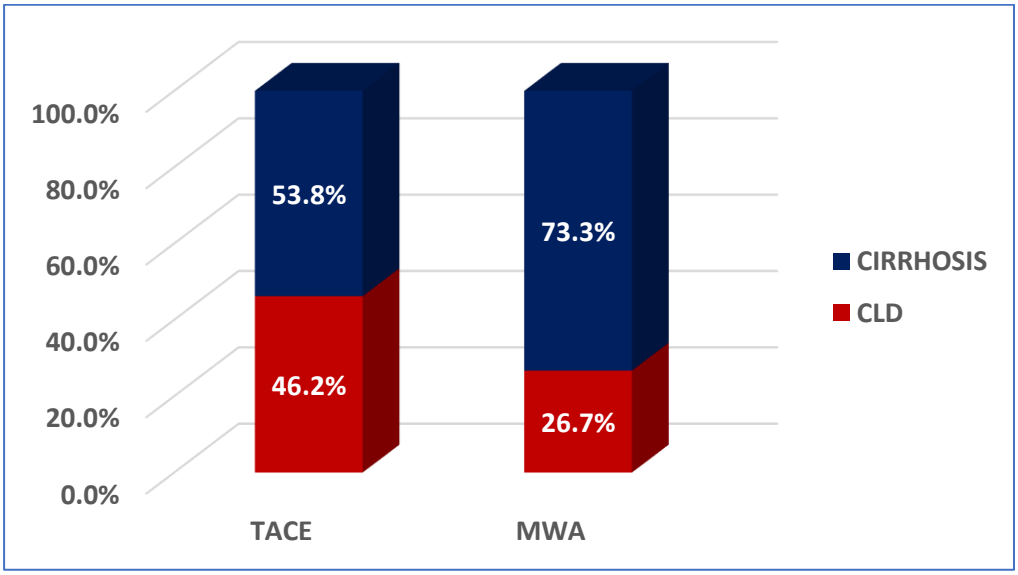
Majority of patients in both study group were identified by surveillance, 10 (76.9%) vs. 9 (60.0%) in TACE and MWA respectively, p = 0.339 (Table9, Fig -9)

3. Diagnosis at time of presentation

TABLE 10: BASIC DIAGNOSIS OF LRT PATIENTS AT THE TIME OF PRESENTATION

BASIC DIAGNOSIS	TOTAL Number (%)	TACE Number (%)	MWA Number (%)	P value
Cirrhosis	18 (64.3%)	7 (53.8%)	11(73.3%)	0.283
Chronic liver Disease (CLD)	10 (35.7%)	6 (46.2%)	4 (26.7%)	

FIG 10: BASIC DIAGNOSIS OF LRT PATIENTS AT THE TIME OF PRESENTATION



The predominant basic diagnosis of patients in both groups at time of diagnosis was cirrhosis, 7 (53.8%) vs. 11 (73.3%0, in TACE and MWA groups respectively. But differences were not statistically significant p = 0.28

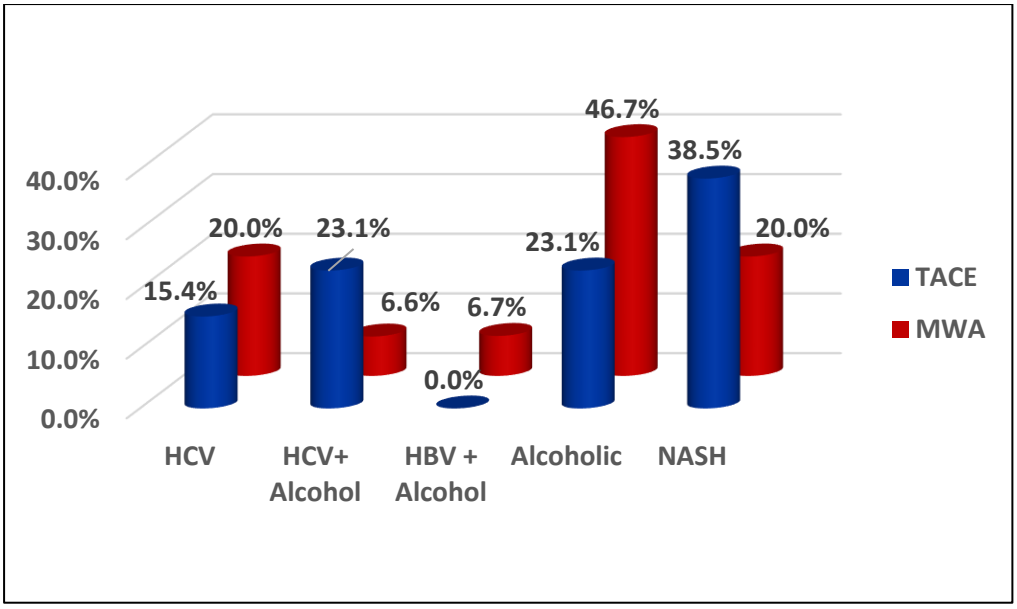
4. Etiology for cirrhosis

The most prevalent risk factor noticed among our patients was alcoholism 3 (23.1%) and 7 (46.7%) in TACE in MWA group respectively. The second prevalent risk factor was NASH, 5 (38.5%) VS. 4 (26.4%) in TACE and MWA group. Only 1(6.7%) patient in MWA group had HBV infection.

TABLE 11: RISK FACTORS FOR CIRRHOSIS IN HCC PATIENTS

ETIOLOGY	TOTAL Number(%)	TACE Number(%)	MWA Number(%)	P value
HCV	5 (17.9%)	2 (15.4%)	3 (20.0%)	0.465
HCV+ Alcohol	4 (14.3%)	3 (23.1%)	1 (6.6%)	
HBV + Alcohol	1 (3.6%)	0	1(6.7%)	
Alcoholic	10 (35.7%)	3 (23.1%)	7 (46.7%)	
NASH	8 (28.6%)	5 (38.5%)	3 (20.0%)	

FIG 11: RISK FACTORS FOR CIRRHOSIS IN HCC PATIENTS



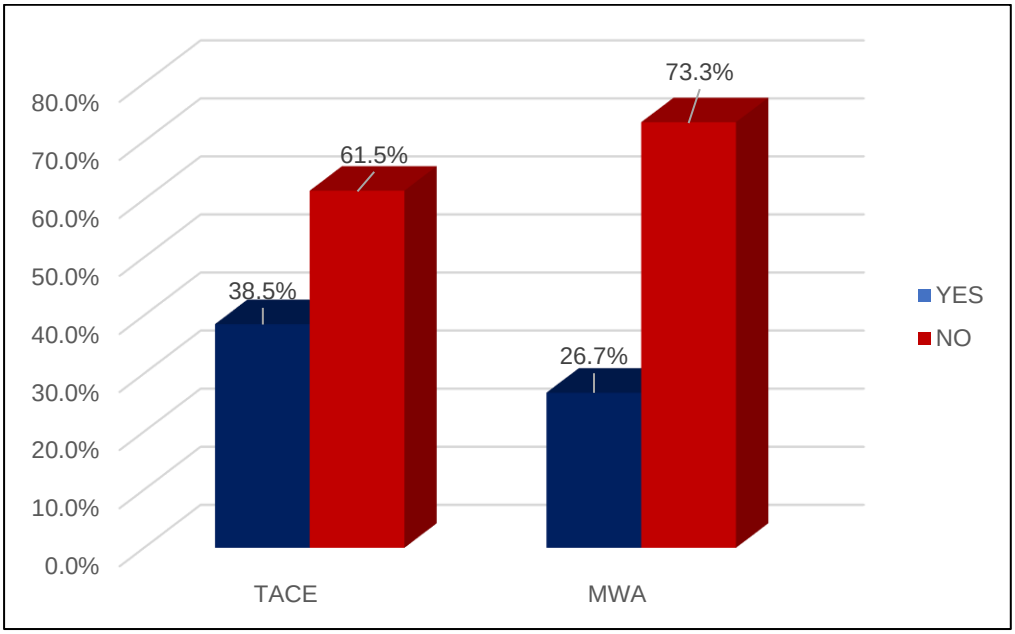
Most prevalent etiological factor was alcoholism followed by non-alcoholic steatohepatitis (NASH). The observations were comparable in the two study groups. P = 0.465. Table 11, Fig 11.

6. Presence of HCV

TABLE 12: PRESENCE OF HCV AMONG LRT PATIENTS

HCV	TACE Number (%)	MWA Number (%)	TOTAL Number (%)	P value
Present	5 (38.5%)	4 (26.7%)	9 (32.1%)	0.794
Absent	8 (61.5%)	11 (73.3%)	19 (67.9%)	

FIG 12: PRESENCE OF HCV AMONG LRT PATIENTS



5 (38.5%) of TACE patients and 4 (26.7%) of MWA patients had HCV. The observation was comparable in both groups, p=0.794.
Table 12, Fig 12.

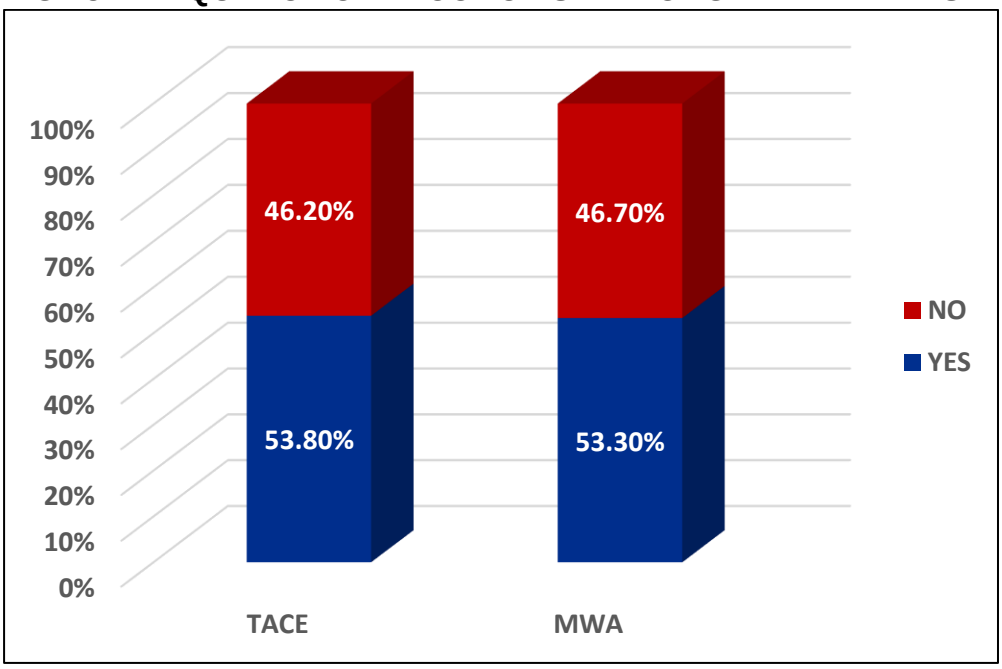
7. Frequency of Alcoholism in LRT

Frequency of alcoholism was comparable in both groups, 5 (53.8%) in TACE vs. 8 (53.3%) in MWA group, p = 0.724. Table 13, Fig- 13.

TABLE 13: FREQUENCY OF ALCOHOLISM AMONG LRT PATIENTS

ALOCHOLISM	TOTAL Number (%)	TACE Number (%)	MWA Number (%)	P value
YES	15 (53.6%)	7 (53.8%)	8 (53.3%)	0.724
NO	13 (46.4)	6 (46.2%)	7 (46.7%)	

FIG 13: FREQUENCY OF ALCOHOLISM AMONG LRT PATIENTS

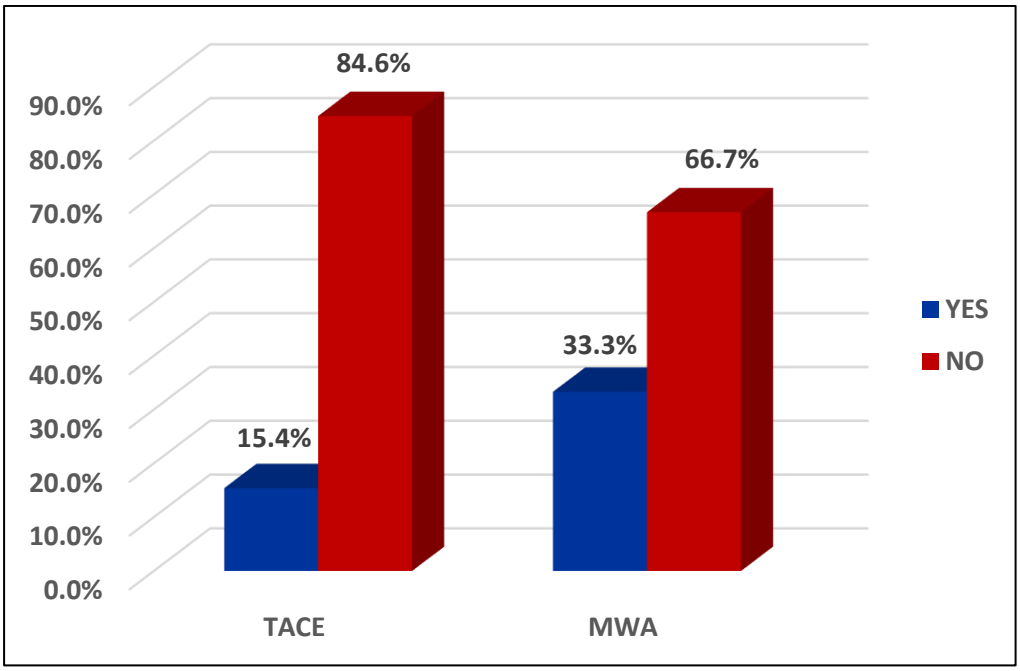


8. Incidence of Smoking in study groups

TABLE 14: INCIDENCE OF SMOKING IN STUDY GROUP

SMOKING	TACE Number (%)	MWA Number (%)	P value
YES	2 (15.4%)	5 (33.3%)	0.274
NO	11 (84.6%)	10 (66.7%)	

FIG 14: INCIDENCE OF SMOKING IN STUDY GROUP



Incidence of smoking as confessed by our patients are shown in Table 14, Fig 14. Occurrence was more in MWA group, 5 (33.3%) compared to TACE group which had only 2 (15.4%) patients addicted to smoking. Difference didn't show statistical significance,p = 0.274.

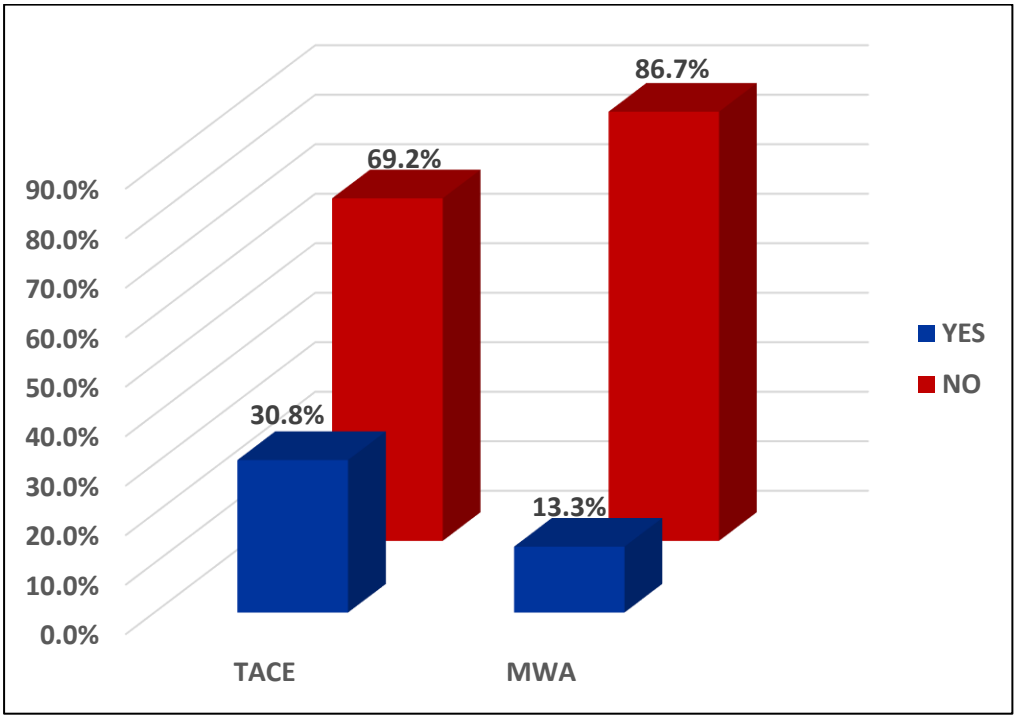
9. Incidence of Opium Abuse

Table15 and Fig-15 delineate the occurrence of opium abuse in study groups.

TABLE 15: INCIDENCE OF OPIUM ABUSE IN STUDY GROUP

OPIUM	TACE Number (%)	MWA Number (%)	P value
Present	4 (30.8%)	2 (13.3%)	0.262
Absent	9 (69.2%)	13 (86.7%)	

FIG 15: INCIDENCE OF OPIUM ABUSE IN STUDY GROUP



Occurrence of opium addiction was observed in 4 (30.8%) vs. 2 (13.3%), in TACE and MWA groups respectively, with no statistical difference, p = 0.262. Table 15, Fig -15.

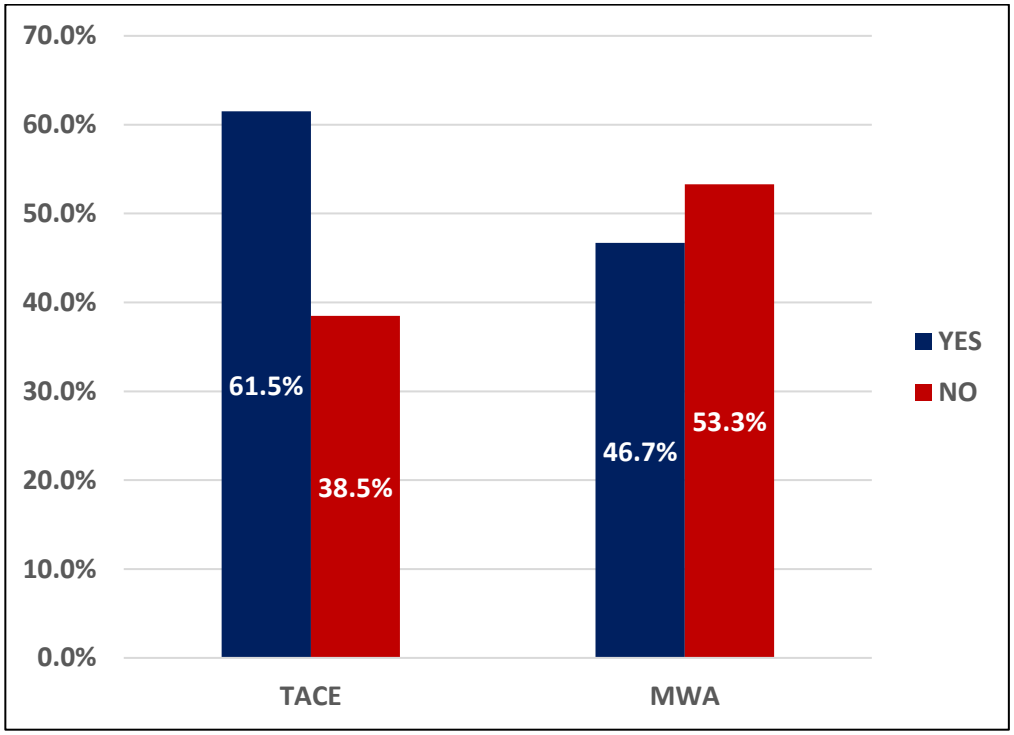
10. Presence of Ascites

Ascites was predominant in TACE group. Table 16. Fig-16.

TABLE 16: PRESENCE OF ASCITES THE STUDY GROUPS

ASCITES	TACE Number (%)	MWA Number (%)	P value
Present	8 (61.5%)	7 (46.7%)	0.431
Absent	5 (38.5%)	8 (53.3%)	

FIG 16: PRESENCE OF ASCITIS THE STUDY GROUPS



Ascites was observed more on TACE group, 8 (61.5%) as compared to 7 (46.7%) in MWA group. The difference was not statistically significant. p=0.431, Table 16. Fig-16.

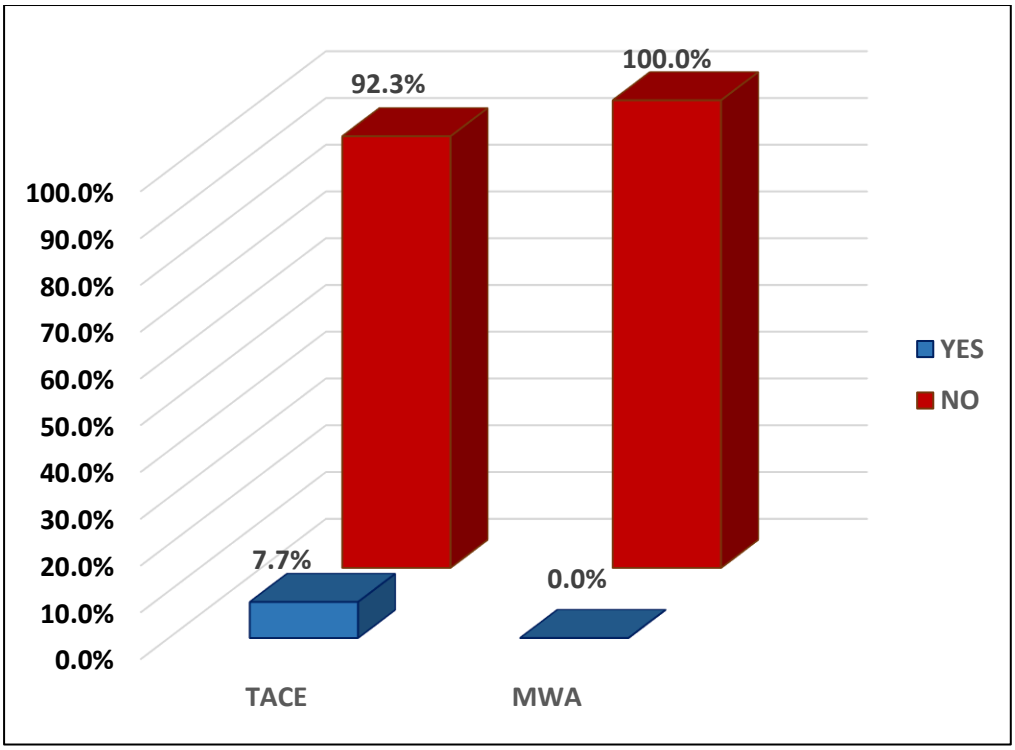
11. Encephalopathy in study groups

One of the patients in TACE group (66-year-old male) had history of encephalitis but the complication resolved before he was considered for TACE.

TABLE 17: PRESENCE OF ENCHAPHALOPATHY IN LRT PATIENTS

ENCEPHALOPATHY	TACE Number (%)	MWA Number (%)	P value
Present	1 (7.7%)	0	0.274
Absent	12 (92.3%)	100%	

FIG 17: THE PRESENCE OF ENCHAPHALOPATHY IN LRT PATIENTS



Only one patient 1 (7.7%) in TACE group had this complication.

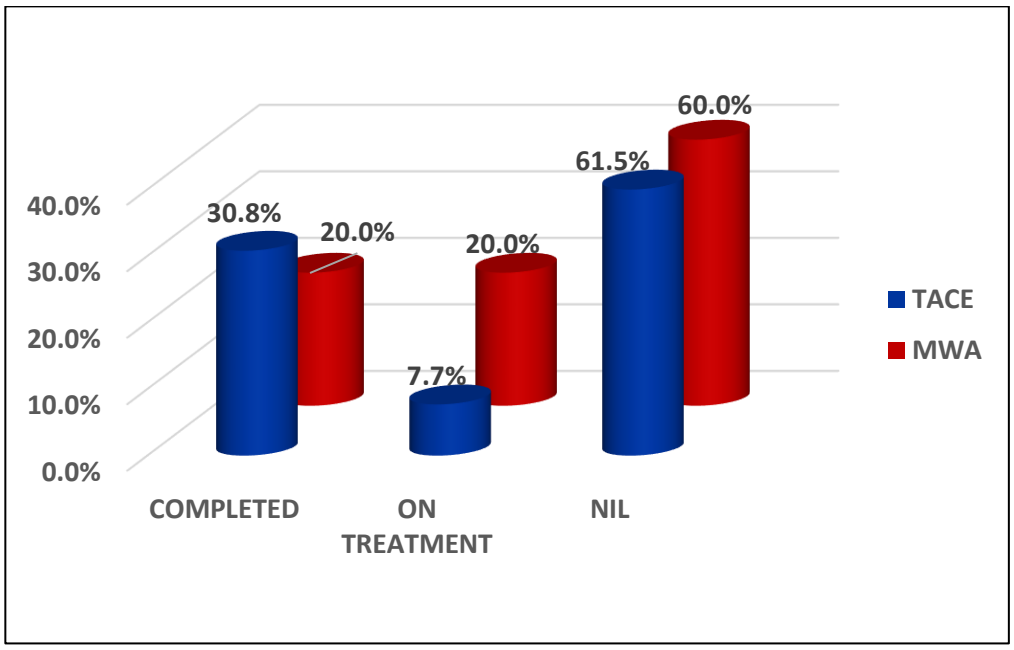
12. Anti-viral Treatment for LRT patients

All 5 (38.5%) patients in TACE group who had HCV, and all patients in MWA group with history of HCV or HBV 6 (40.0%) underwent antiviral treatment. Table -18, Fig 18.

TABLE 18: ANTIVIRAL TREATMENT FOR LRT PATIENTS

ANTIVIRAL TREATMENT	TACE Number (%)	MWA Number (%)	P value
On treatment	1 (7.7%)	3 (20.0%)	0.587
Completed	4 (30.8%)	3 (20.0%)	
None	8 (61.5%)	9 (60.0%)	

FIG 18: ANTIVIRAL TREATMENT FOR LRT PATIENTS



4 (30.8%) vs. 3 (20.0%) patients completed anti-viral treatment, and 1(7.7% vs. 3 (20.0%) patients were currently on anti-viral treatment in TACE group and MWA group respectively. P= 0.587

8 (61.5%) and 9 (60.0%) in TACE and MWA groups did not have HCV or HBV and were not considered for anti-vital therapy. Table 18, Fig -18

13. Biochemistry

TABLE 19: COMPARISON OF MEAN (SD) 0F HEMATOLOGICAL AND BIOCHEMICAL PARAMETERS

PARAMETRS	TACE Mean (SD)	MVA Mean (SD)	P value
Hb (gm/dL)	10.7 (1.9)	10.57 (2.1)	0.850
CBC (10^3 /µl)	8.04 (13.1)	4.98 (2.2)	0.381
Platelet (10^3 /µl)	136.1(78.6)	104.8 (59.1)	0.240
Total Albumin (g/dl)	3.98 (1.89)	3.47 (0.59)	0.388
Total Protein (g/dl)	11.16 (17.1)	6.76 (0.76)	0.328
SGOT (U/L)	80.62 (56.6)	67.53 (51.9)	0.529
SGPT (U/L)	68.00 (69.3)	43.73 (25.7)	0.218
Alk, Phosphatase (U/L)	162.15 (118.3)	178.47 (117.5)	0.718
Total Bilirubin (mg/dl)	1.65 (2.29)	1.19 (0.67)	0.461
Serum Urea (mg/dl)	26.85 (15.42)	29.27 (16.74)	0.696
Serum Creatinine (mg/dl)	0.80 (0.17)	0.82 (0.36)	0.851
INR	1.34 (0.15)	1.29 (0.23)	0.581
AFP ng/mL	150 (20.7)	80.5 (15.7)	0.724

No statistical difference was observed in biochemical parameters between the two groups.

TABLE 20: COMPARISON OF PROPORTIONS REGARDING LIVER FUNCTION TESTS IN LRT PATIENTS

PARAMETERS	TACE Number (%)	MWA Number (%)	TOTAL Number deranged (%)	P value
T. Bilirubin mg/dL				
<1.5	6 (46.2%)	7 (46.7%)		0.724
≥1.5	7(53.8%)	8 (53.3%)	15 (53.6%)	
Serum SGOT (U/L)				
>45	6 (46.2%)	7 (46.7%)	13 (46.4%)	0.724
≤45	7(53.8%)	8 (53.3%)		
Serum SGPT (U/L)				
>40	8 (61.5%)	6 (40.0%)	14 (50.0%)	0.449
≤40	5 (38.5%)	9 (60.0%)		
Serum Alk.Pase (U/L)				
<220	9 (69.2%)	10 (66.6%)		0.794
≥220	4 (30.8%)	5 (53.3%)	9 (32.1%)	
Serum Albumin (g/dl)				
<3.0	3 (23.1%)	3 (20.0%)	6 (21.4%)	0.792
≥3.1	10(76.9%)	12 (80.0%)		
Serum AFP ng/mL				
<44	2 (15.4%)	4 (26.7%)		0.274
≥44	6 (46.2%)	2 (13.3%)	8 (33.3%)	

Abbreviations: Alk. Pase-Alkaline Phosphatase, AFP- Alpha feto protein

Hyperbilirubinemia was observed in 6 (46.2%) and 7 (46.7%) of TACE and MWA patients respectively, p= 0.724

No statistical difference was recorded among patients who had altered SGOT, SGPT and Alk. Pase levels.

3 (23.1%) and 2 (20.0%) patients had albumin less than 3 gm% in TACE and MWA groups, respectively

Serum AFP levels ranged from 8.7 to 366 ng/mL. One patient in TACE group had AFP value > 3000 ng/mL.

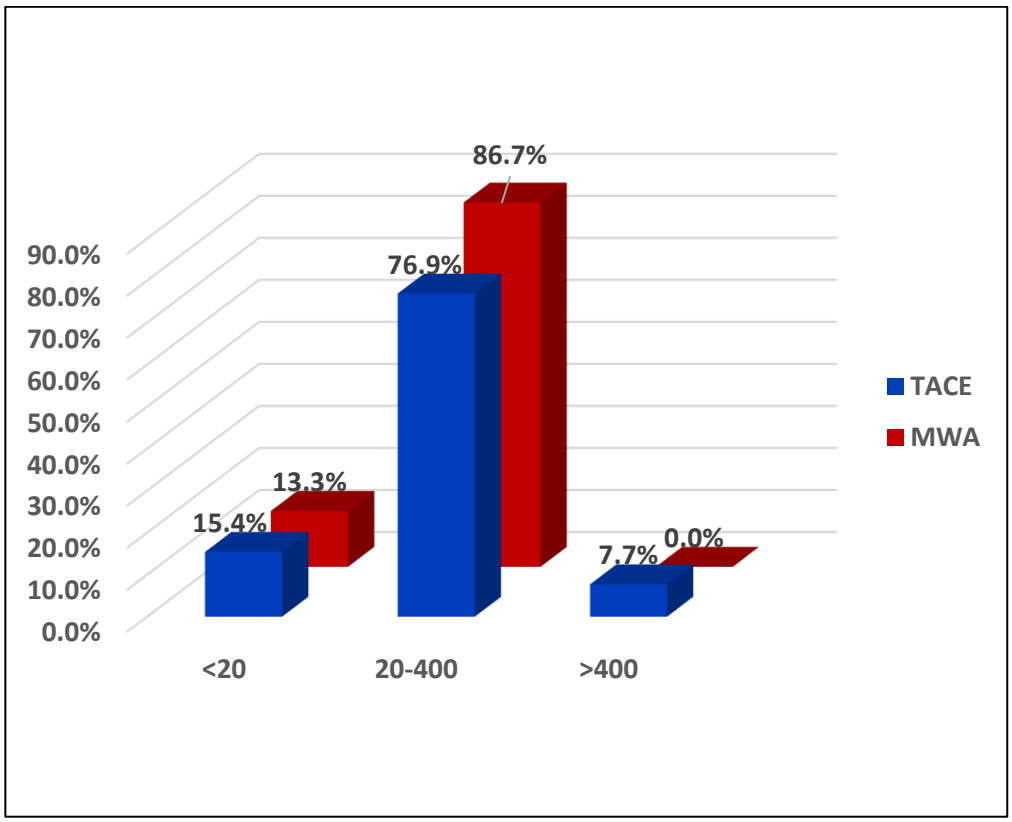
AFP value > 44 was documented more in TACE patients, 5 (38.5%) vs. 2 (13.3%) MWA patients, respectively. But difference was not statistically significant

14. Alpha fetoptotein (AFP)

TABLE 21: SERUM AFP LEVELS IN LRT PATENTS

AFP	TACE Number (%)	MWA Number (%)	P value
>400ng/ml	1 (7.7%)	0	0.724
21-400 ng/ml	5 (38.5)	6 (40.0%)	
≤ 20 ng/ml	2 (15.4%)	2 (13.3%)	

FIG 19: SERUM AFP LEVELS IN LRT PATENTS



AFP value was not available for all patients. Only one patient among TACE patients had AFP levels > 400 ng/ml, the value was > 3000 ng/ml. None in MWA group had APP more than 400 ng/ml

There was no statistical significance was observed between the two groups in relation to alpha fetoprotein levels. p = 0.724

CLASSIFICATION OF HCC

15. CHILD-PUGH Classification

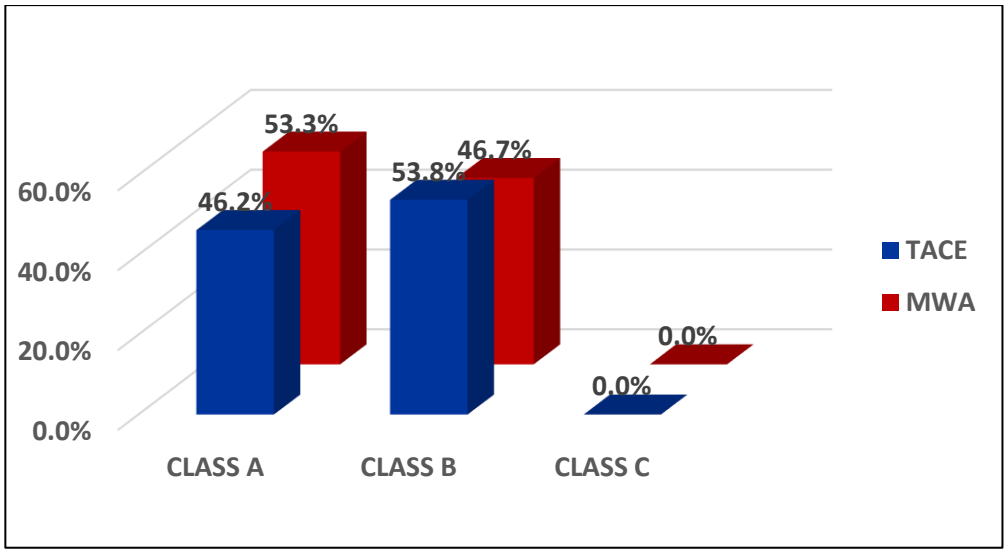
The severity of CLD/ cirrhosis and liver function status of the patient was scored objectively using the Child-Pugh classification, based on total bilirubin, serum albumin, INR, presence of ascites or hepatic encephalopathy. The number of cases that were categorised as Child Pugh class A, B and C are shown in Table 22, Fig -20

The Child-Pugh (CP) classification among LRT patient groups were comparable. 50% were included in Class A, 50.0 % in Class B.

TABLE 22: CHILD-PUGH CLASSIFICATION OF LRT PATIENTS

CHILD-PUGH	TACE NO. (%)	MVA NO. (%)	TOTAL NO.%	P value
CLASS A	6 (46.2%)	8 (53.3%)	14 (50.0%)	0.477
CLASS B	7 (53.8%)	7(46.7%)	14 (50.0%)	
CLASS C	0	0	0	

FIG 20: CHILD-PUGH CLASSIFICATION OF LRT PATIENTS



There were 6 (46.2%) and 8 (53.3%) in Class A category and 7 (53.8%) vs. 7 (46.7%) were included in Class B category in TACE and MWA patients respectively. P= 0.477

CP classification was comparable in both TACE and MWA groups, p = 0.477.

16. BCLC Staging

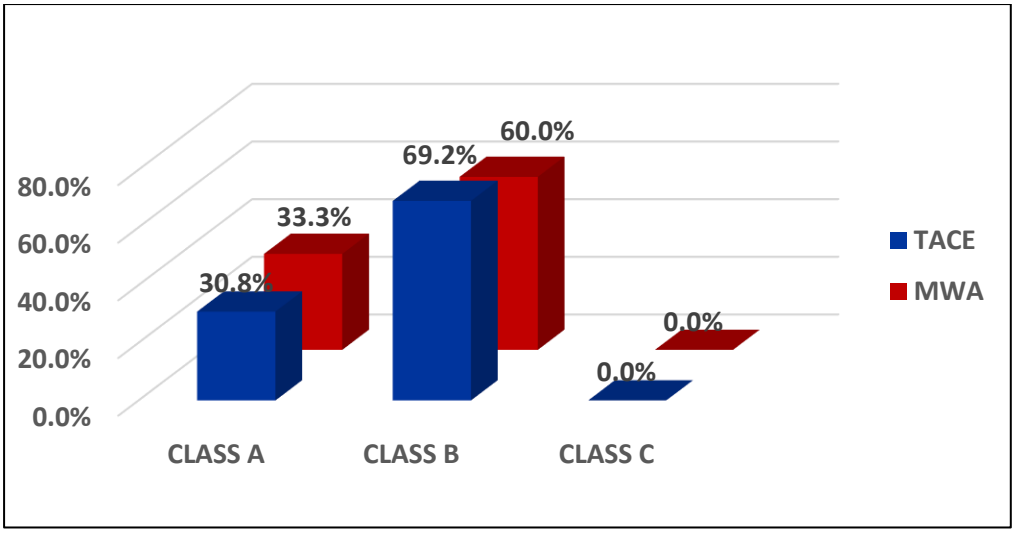
The BCLC stages of all the cases were calculated depending on the ECOG performance status, Child-Pugh score, and radiologic tumor extent (number of tumors, tumor size, vascular invasion, nodal and extrahepatic spread).

There was a total of 1 (3.6%), 9 (32.1%), 18 (64.3%), in stages 0, A, and B, respectively in BCLC stages of our study group.

TABLE 23: BCLC STAGING OF LRT PATIENTS

BCLC STAGE	TACE NO. (%)	MVA NO. (%)	TOTAL NO. (%)	P value
Very early Stage 0	0	1 (6.6%)	1 (3.6%)	0.076
A (Early Stage)	4 (30.8%)	5 (33.3%)	9 (32.1%)	
B (intermediate Stage)	9 (69.2%)	9 (60.0%)	18 (64.3%)	
Stage C Advanced	0	0	0	
Stage D, End Stage	0	0	0	

FIG 21: BCLC STAGING OF THE CASES



There were 4 (30.8%) vs.5 (33.3%) in stage A category in TACE and MWA groups respectively.

Similarly, 9 (69.2%) vs. 9 (60.0%) were observed among TACE and MWA group respectively.

In MWA group, there were 1(6.7%) patient in stage 0

But differences were not statistically significant p = 0.076.

17. MELD Score

Model for End stage Liver Disease (MELD) scores of the patients were calculated using their serum bilirubin, creatinine and INR levels. The score ranged from 7 to 20 in our study groups.

TABLE 24: MODEL FOR END-STAGE LIVER DISEASE (MELD) OF LRT PATIENTS

MELD	TACE NO. %	MWA NO. %
7	1 (7.7%)	2 (13.3%)
8	1 (7.7%)	2 (13.3%)
9	3 (23.1%)	2 (13.3%)
10	1 (7.7%)	1 (6.7%)
11	4 (30.8%)	0
12	0	4 (26.7%)
13	0	2 (13.3%)
14	1 (7.7%)	1 (6.7%)
15	1 (7.7%)	0
18	0	0
19	1 (7.7%)	0
20	0	1 (6.7%)

FIG 22: MODEL FOR END-STAGE LIVER DISEASE (MELD) OF LRT PATIENTS

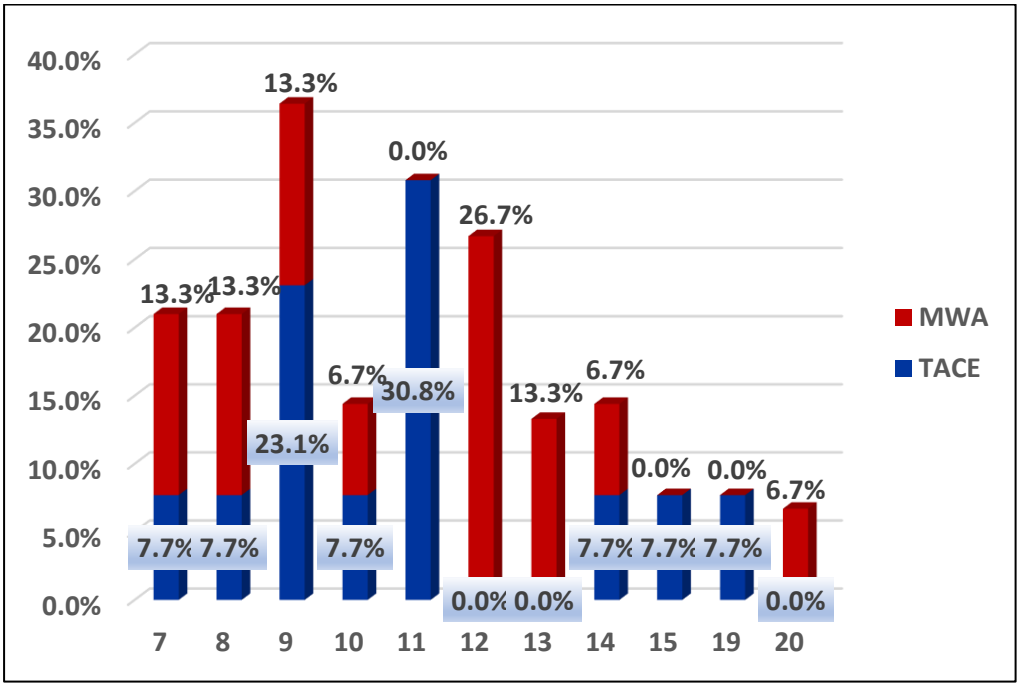
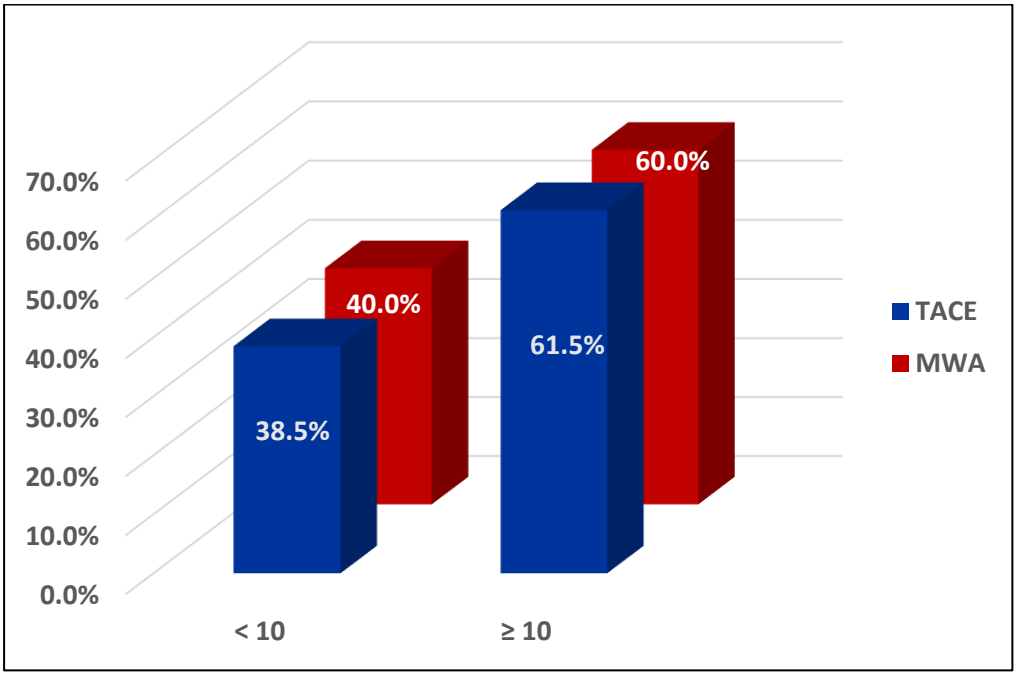


TABLE 25: PROPORTION OF MODEL FOR END-STAGE LIVER DISEASE (MELD) SCORE IN LRT PATIENTS

MELD	TACE NO. (%)	MWA NO. %	P value
<10	5 (38.5%	6 (40.0%)	0.761
≥ 10	8 (61.5%)	9 (60.0%)	

FIG 23: PROPORTION OF MODEL FOR END-STAGE LIVER DISEASE (MELD) SCORE IN LRT PATIENTS



A MELD score of more than 10 was observed in 8 (61.5%) and 9 (60.0%) in TACE and MWA groups respectively. The observations were comparable in both groups. P = 0.761

TUMOR CHARACTERISTICS

18. Tumor number

Maximum number of HCC lesions considered for treatment in our study group was 4. Single lesion was observed in 19 patients (9 TACE patients

and 10 MWA patients). Details of lesion numbers before treatment is documented in Table-26, Fig- 24.

TABLE 26: TOTAL NUMBER OF HCC LESIONS BEFORE TREATMENT

NO OF LESION	NO OF CASES	TACE NO. %	MWA NO. %	P VALUE
1	19	9 (69.2%)	10 (66.7%)	0.177
2	3	0	3 (20.0%)	
3	4	2 (15.4%)	2 (13.3%)	
4	2	2 (15.4%)	0	

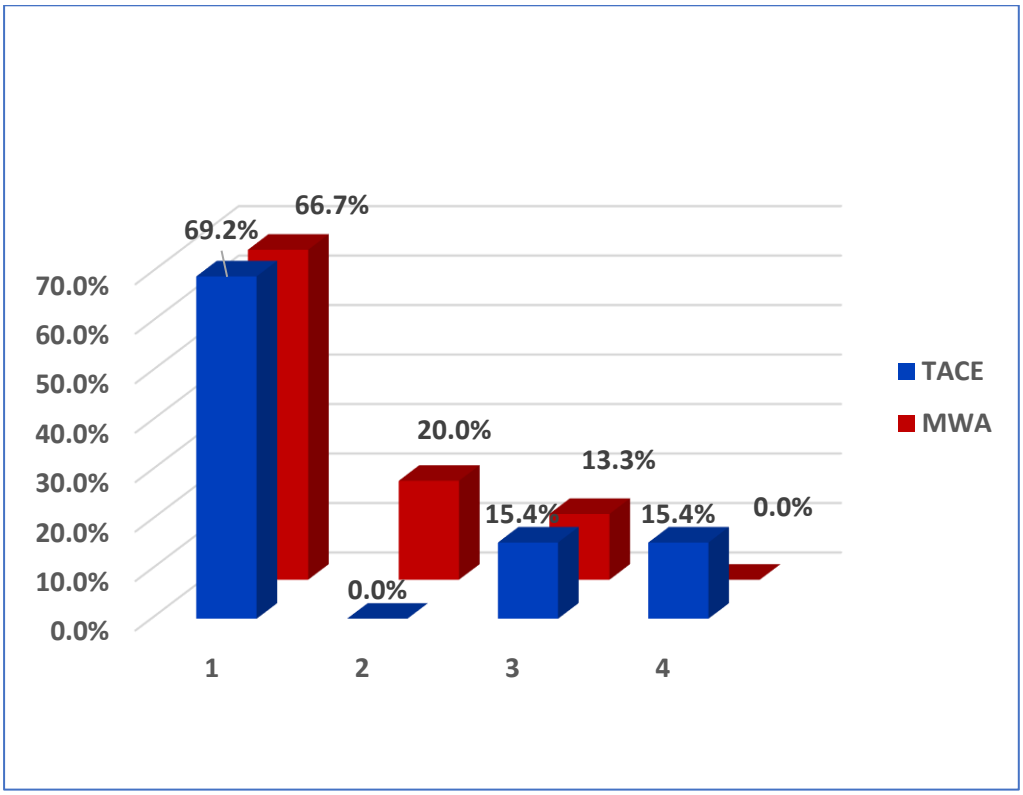
19 patients had 1 lesion, 9 (69.2%) in TACE and 10 (66.7 %) in MWA patients.

2 lesions were observed in 3 (20.0%) of MWA patients.

3 lesions were documented in 4 patients, 2 (15.4%) and 2 (13.3%) in TACE and MWA groups, respectively. The maximum number of lesions treated in MWA group was 3.

4 lesions were recorded in 2 (15.4%) patients who had TACE procedure.

FIG 24: TOTAL NUMBER OF HCC LESIONS BEFORE TREATMENT



1 lesion was documented in 19 patients (9 TACE and 10 MWA patients)

2 lesions observed in 3 patients who underwent MWA.

3 lesions in 2 TACE and 2 MWA patients.

4 lesions noted in 2 TACE patients.

No statistical difference was there regarding number of lesions between the two study groups. P= 0.177.

Total number of lesions treated were 45, 23 lesions in TACE patients and 22 lesions in MWA patients.

19. The Couinaud segments

The Couinaud segments involved by the lesions were identified on the baseline CT/MRI and are tabulated, Table 27 and Figure 25.

TABLE 27: COUINAUD SEGMENTS FOR LESIONS BEFORE TREATMENT

COUINAUD SEGMENTS	TOTAL NO OF CASES	TACE No. (%)	MWA No. (%)
I,VI	1	0	1 (6.7%)
II,VIII/V,VI	1	1(7.7%)	0
II/III	1	0	1 (6.7%)
IV	1	0	1 (6.7%)
IV B	1	0	1 (6.7%)
V,VI, VIII	1	1 (7.7%)	0
V/VIII	1	1 (7.7%)	0
VI	4	2 (15.4%)	2 (13.3%)
VI,II,VI	1	0	1 (6.7%)
VI,IV,VII	1	1 (7.7%)	0
VI,V/VIII,IVa	1	1 (7.7%)	0
VI/VII, VIII,VIII	1	0	1 (6.7%)
VII	3	1 (7.7%)	2 (13.3%)
VII, VI	1	1 (7.7%)	0
VII/VI	1	1 (7.7%)	0
VIII	5	1 (7.7%)	4 (26.7%)
VIII,III, VIII	1	1 (7.7%)	0
VIII,V,I	1	1 (7.7%)	0
VIII,VI	1	0	1(6.7%)

Segmental distribution of the lesions identified on imaging is shown above in Table 27. The most frequent Couinaud segment involved was segment VI, with a total of 13 lesions, followed by segment VIII with 11 lesion and segment V with 6 lesions.

20. LI-RADS diagnosis of the lesions

All the lesions treated were diagnosed as either LI-RADS 5 (definitely HCC) or LI-RADS 4 (probably HCC) and single case of LR-TIV (tumor in vein) in the CT/MRI triphasic imaging done prior to the procedure, Table 28.

TABLE - 28: LI-RADS OF ALL LESIONS DOCUMENTED BEFORE TREATMENT

LI-RADS	BEFORE RX LESION-1		BEFORE RX LESION-2		BEFORE RX LESION-3	
	TACE NO (%)	MWA NO (%)	TACE NO (%)	MWA NO (%)	TACE NO (%)	MWA NO (%)
LR-3			1(7.7%)		1(7.7%)	0
LR -4			1(7.7%)	2(13.3%)		
LR-5	12(92.3%)	15 (100%)	4(30.8%)	2(13.3%)	3(23.1%)	2 (13.3%)
LR-TIV	1 (7.7%)	0				

For First lesion all lesions 15 (100%) were LR-5 lesions in MWA group vs 12 (92.3%) LR-5 and 1 (7.7%) LR-TIV lesions in TACE group.

Regarding Lesion-2, there were 1(7.7%) and 2 (13.3%) LR-4 lesions in TACE and MWA groups.

Similarly, there were 4 (30.8%) and 2 (13.3%) LR-5 lesions in TACE and MWA groups respectively.

In Lesion 3, there were 3 (23.1%) and 2 (13.3%) LR-5 lesions in TACE and MWA groups respectively.

TABLE 29: LI-RADS OF LESIONS - 6 WEEKS POST TREATMENT

LI-RADS	6WEEKS AFTER RX LESION-1		6WEEKS AFTER RX LESION-2		6 WEEKS AFTER RX LESION-3	
	TACE NO (%)	MWA NO (%)	TACE NO (%)	MWA NO (%)	TACE NO (%)	MWA NO (%)
LR -4	1(7.7%)		1 (7.7%)			
LR-3					3(23.1%)	
LR-TR VIABLE	10(76.9%)	I (6.7%)	2(15.4%)	1 (6.7%	2(15.4%)	1 (6.7%)
LR-TR NONVIABLE	2 (15.4%)	12(80.0%)	1 (7.7%)	3 (20.0%)	1 (7.7%)	1 (6.7%)
LR-TR EQUIVOCAL		1 (6.7%)				
0		1 (6.7%)	8 (61,5%)	11(73.3%)		
NEW LESION LR-5			1 (7.7%)			

At 6 weeks review after LRT, for the first lesion there were 10 (76.9%) vs. 1 (6.7%) viable lesions in TACE and MWA respectively. Similarly, there were 2 (15.4%) vs.12 (80.0%) non-viable lesions in TACE MWA groups respectively, The difference was highly significant, **p=0.001**.

For second lesion, there was 1(7.7%) LR-4 lesion, 2 (15.4%) LR-TR viable lesions, 1 (7.7%) LR-5 new lesion, vs. 1 (6.7%) LR-TR viable and 3 (20.0%) LT-TR non-viable lesions MWA group.

For third lesion there were 2 (15.4%) and 1(6.7%) LR-TR viable lesions in TACE and MWA groups respectively.

21. Tumor Size

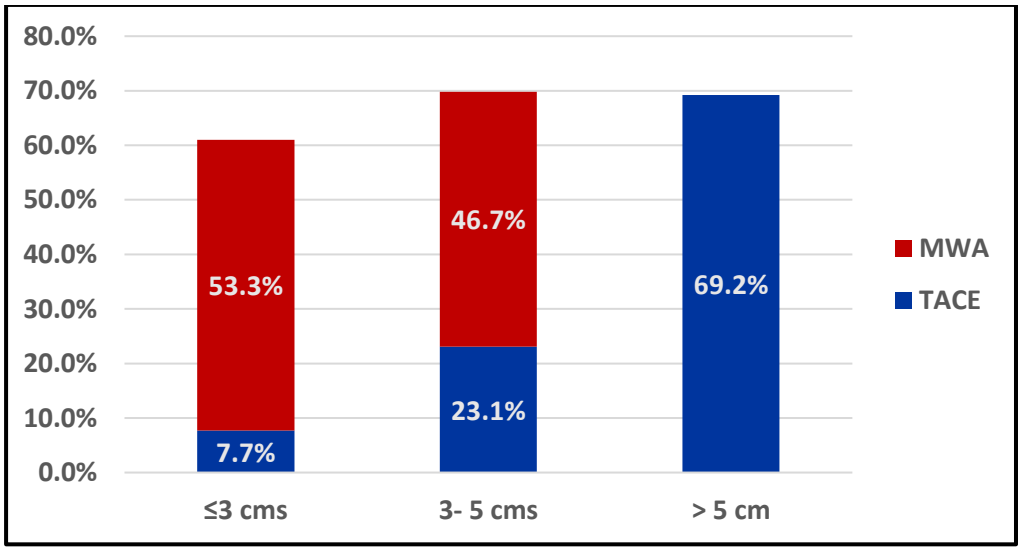
TABLE 30: TUMOR SIZE BEFORE TREATMENT

Tumor Size	TACE NO. (%)	MVA NO. (%)	P value
≤ 3 cms	1 (7.7%)	8 (53.3%)	**0.001**
3-5 cms	3 (23.1%)	7(46.7%)	
>5 cms	9 (69.2%)	0	
Total	13 (100%)	15 (100%)	

Tumor size in TACE group before treatment ranged from 1.3 x 1.1 cms to 12.1 x 10.14 cms, where as tumor size in MWA group ranged from 0.8 cms x 0.8 cms to 5.5 x 5.0 cms. In one patient in TACE group lesion was described as large, multiple and nodulated nodules.

Tumor size > 5 cms was recorded in 9 (69.2%) in TACE group vs. (0%) in MWA group. Tumor size 3-5 cms were, 3 (23.1%) and 7 (46.7%) in TACE and MWA group respectively. Tumor size of ≤ 3 cms were observed in 1 (7.7%) and 8 (53.3%) in TACE and MWA groups, difference was highly significant, p= 0.001.

FIG 25: TUMOR SIZE BEFORE TREATMENT



Tumor size > 5 cms was seen 69.2% in TACE and none in MWA group.

22. Metastasis

2 (15.4%) patients in TACE group developed metastasis.

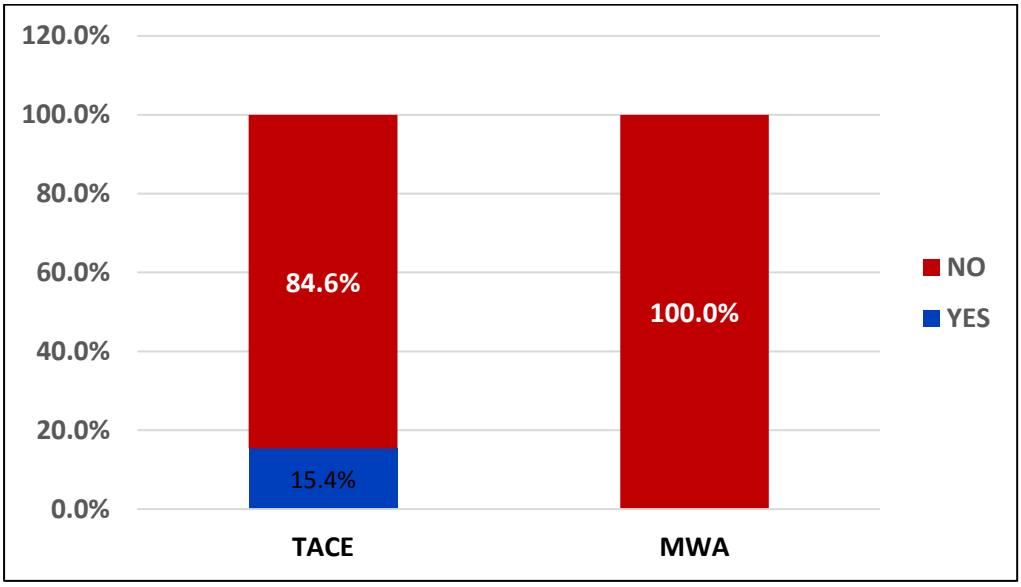
Site of metastasis was pulmonary and vertebral.

None in MWA group had this complication.

TABLE 31: METASTASIS IN TACE PATIENTS

Site	TACE NO. %	MWA
YES	2 (15.4%)	0
NO	11 (84.6%)	15 (100%)

FIG 26: INCIDENCE OF METASTASIS



2 patients in TACE group had metastasis.

Response to treatment

23. mRECIST at 6weeks after treatment

The overall patient response to LRT at 6 weeks was analysed by mRECIST.

One patient in MWA group died during procedure due to bleeding.

Complete remission (CR) was observed in 11 (73.3%) in MWA group vs. 2 (15.4%) in TACE group.

Partial remission (PR)was observed in 2 (15.4%) TACE patients, none in MWA group.

Stable disease (SD) was recorded in 4 (30.8%) and 1 (6.7%) patients in TACE and MWA group respectively.

And Progressive disease (PD) was documented in 5 (38.5%) and 2 (13.3%) patients in TACE and MWA groups respectively.

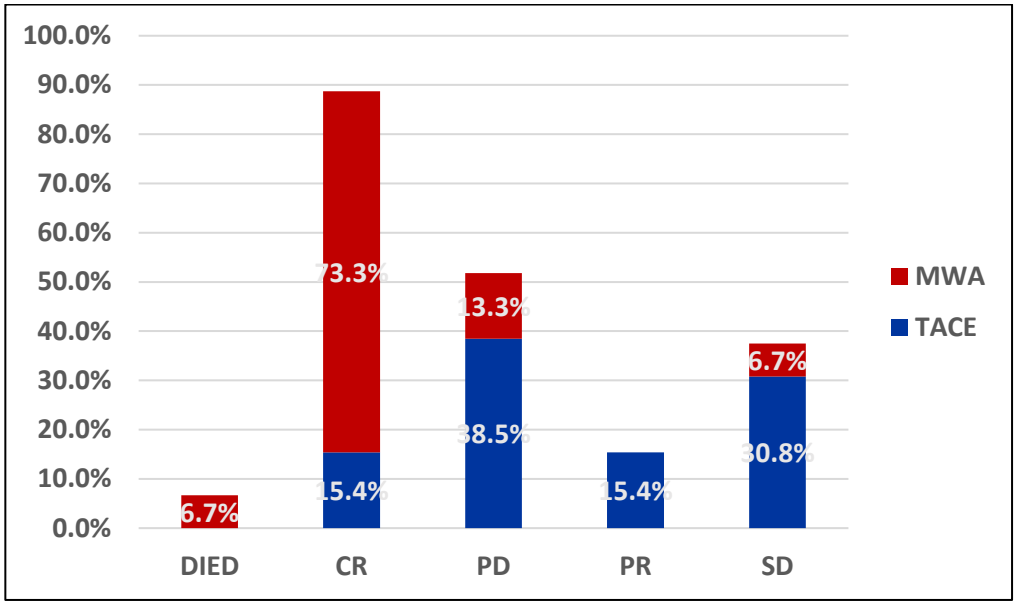
The differences were statistically different p= 0.016

Worse outcome was evident among TACE patients compared to those who underwent MWA.

TABLE 32: RESPONSE TO TREATMENT AT 6 WEEKS FOLLOW UP BY mRECIST

mRECIST At 6 WEEKS	**TACE NO. (%)**	**MWA NO.(%)**	**P value**
Died	0	1 (6.7%)	**0.016**
CR (Complete remission)	2 (15.4%)	11 (73.3%)	
PR (Partial remission)	2 (15.4%)	0	
SD (Stable disease)	4 (30.8%)	1 (6.7%)	
PD (Progressive disease)	5 (38.5%)	2 (13.3%)	

FIG 27: RESPONSE TO TREATMENT AT 6 WEEKS FOLLOW UP BY mRECIST



73.3% of patients in MWA group had complete remission

38.5%, 15.4 patients and 30.8% of patients in TACE group had progressive disease, partial remission and stable disease respectively.

Only 13.3% and 6.7% of patients among MWA group had progressive disease and stable disease respectively.

Differences were statistically significant. p = 0.016

24. mRECIST 3 months after treatment

Complete tumor remission was observed more after MWA than TACE, 60.0% vs. 23.1% respectively.

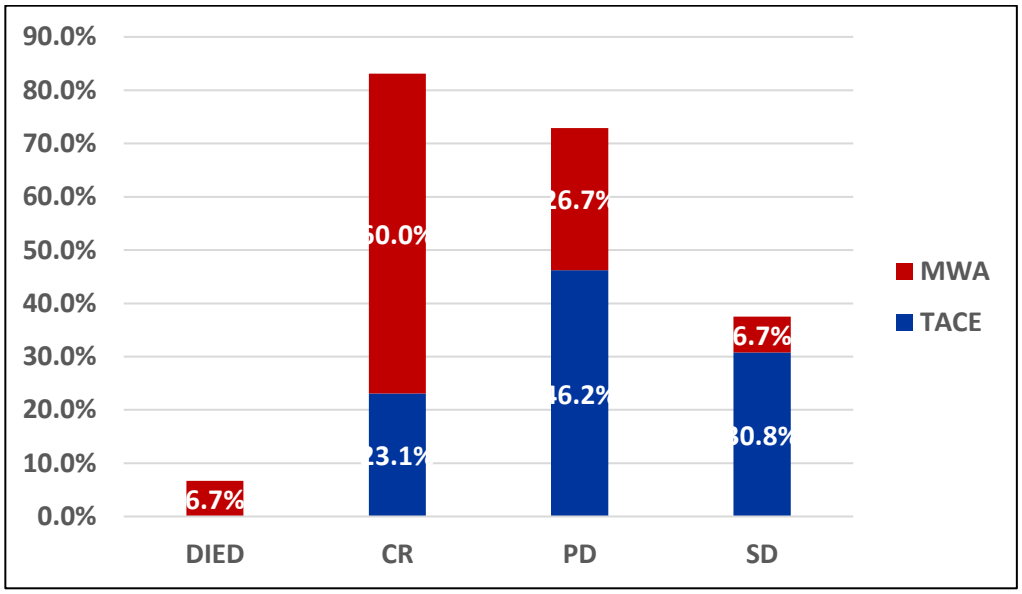
Progressive disease and stable disease were seen more in TACE group, 46.2% and 30.8% respectively vs. 4 (27.7%) and 1 (6.7%) respectively among MWA subjects.

But differences did not show statistical difference. p= 0.107

TABLE 33: RESPONSE TO TREATMENT BY mRECIST AT 3 MONTHS

mRECIST after 3 months	TACE NO. (%)	MWA NO. (%)	P value
Died	0	1 (6.7%)	0.107
CR (Complete remission)	3 (23.1%)	9 (60.0%)	
SD (Stable disease)	4 (30.8%)	1 (6.7%)	
PD (Progressive disease)	6 (46.2%)	4 (27.7%)	

FIG 28: RESPONSE TO TREATMENT BY mRECIST AT 3 MONTHS



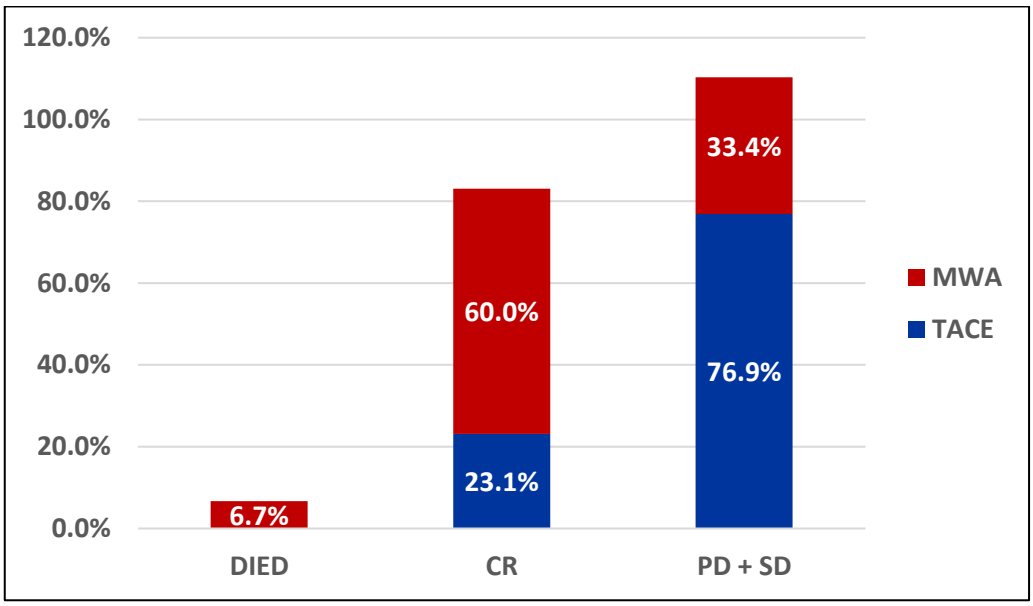
25. Response at 3 months, reviewed

3 months outcome was recalculated, after combining (Partial response and Stable disease) and matched against Complete Remission

TABLE 34: AMENDED RESPONSE TO LRT BY mRECIST AT 3 MONTHS

mRECIST-3 months	TACE NO. %	MWA NO. %	P value
Died	0	1(6.7%)	0.112
CR	3 (23.1%)	9 (60.0%)	
PD+SD	10 (76.9%	5 (33.4%)	

FIG 29: AMENDED RESPONSE TO LRT BY mRECIST AT 3 MONTHS



At 3 months, there was complete remission in 60.0% of MWA patients. (Progressive disease plus stable disease) in TACE patients came up to 76.9%. The difference still did not give statistical significance, p=0.112

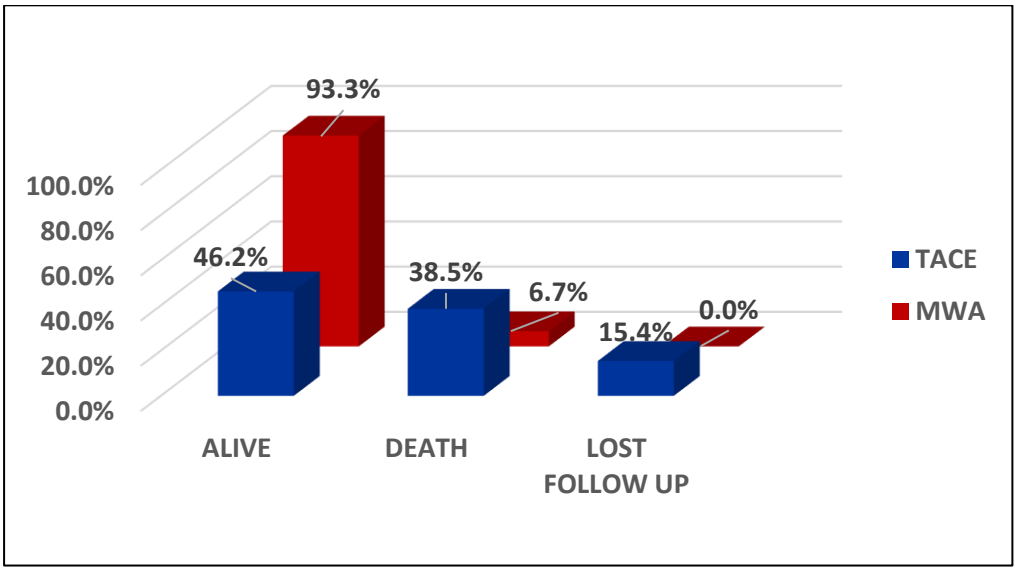
26. Out come regarding survival

Survival out-come between the 2 LRT patient groups were obvious. Follow up after 6 months period documented 14(93.3%) vs. 6 (46.2%) live patients in MWA vs. TACE group respectively. Death happened in 5 (38.5%) patients in TACE, but only 1 (6.7%) in MWA group. 2 (15.4%) patients were lost to follow up. The differences were statistically significant, **p = 0. 019**

TABLE 35: SURVIVAL OUTCOME IN LRT PATIENTS

OUTCOME	TACE NO. (%)	MVA NO.(%)	TOTAL NO. (%)	P VALUE
Alive	6 (46.2%)	14 (93.3%)	20 (71.4%)	**0.019**
Death	5 (38.5%)	1 (6.7%)	6 (21.4%)	
Lost Follow up	2 (15.4 %)	0	2 (7.1%)	

FIG 30: SURVIVAL OUTCOME IN LRT PATIENTS



93.3% patients in MWA group were alive after follow up period vs. 46.2% in TACE group. Death happened in 38.5% patients who underwent TACE vs. 6.7% in MWA group.

MULTIVARIATE COX REGRESSION ANALYSIS:

Patients were classified in responders (complete and partial response) and non-responders (stable and progressive disease).

And a multivariate analysis was done using the following predictors that can affect outcome.

Age <60, ≥60

Gender M/F

Detection by survillence or not

Risk factor alcohol/ not

Risk factor HCV/ not

AFP ≥ 400/ < 400 ng/ml

Bilirubin>1.6 ng/ml/≤

Albumin< 3.3/ ≥3.3 g/

C-P grading A/ B

BCLC score A/ B

MELD Score <10/≥10

Tumor number 2/ > 2

Tumor size 5/ >5 cms

None of the factors proved to be an independent risk factor for worse tumor response to treatment.

COMPLICATIONS DOCUMENTED IN LRT PATIENTS

- Death happened in 1 (60.7%) MWA patient because of bleed into postablation cavity. Only one death was documented in MWA group
- Death happened in 5 (38.5%) in TACE group, all had decompensated cirrhosis, few with other comorbidities.
- 2 (15.4%) patients in TACE group had metastasis (pulmonary nodules and vertebra) These patients also died.
- Vascular thrombosis developed in 3 (23.1%) TACE patients (Main portal vein plus splenic vein, Right branch of portal vein and right hepatic vein etc were the sites involved)
- Recanalization of umbilical vein seen in 2 (15.4%) TACE patients
- Total 15 patients, 8 (61.5%) and 7 (46.7%) in TACE and MWA group had ascites.
- Only 1 (7.7%) among TACE patients had encephalitis. (Resolved before treatment).
- 9 (69.3%) patients developed portal hypertension in TACE group.

DISCUSSION

This single-center prospective and retrospective study included a total of 28 patients with HCC; 13 (46.4%) treated by transarterial chemoembolization (TACE) and 15 (53.6%) who underwent MWA procedures. Patient stratification and treatment allocation are based on tumor stage, liver function, and performance status, according to the Barcelona Clinic Liver Cancer (BCLC) staging system. The response was evaluated on preprocedural and postprocedural CT by using mRECIST assessment method and the response was classified as progressive disease, stable disease, partial response and complete response. The patients were registered in department of Radio-Diagnosis, Dayanand Medical College and Hospital, a teaching medical institution in Punjab, North India. The study done over a period of three years.

In addition to determining the outcome, we also explored the different factors that can affect the outcome in this population group. This topic was chosen in view of the increasing prevalence of HCC in our country and the large body of literature which suggest the evolution of LRTs that increase survival in HCC patients and presents a challenge for the treating physician and interventional radiologist.

Age of our patients ranged from 46 to 84 years with mean of 60.7 years. The maximum number of patients in the study were in the age group 51 – 70 years, 22 (78.6%) which is comparable to results published by other authors from India in single center studies. They reported that the median age of presentation of Indian patients with liver cancer has been noted to be 40-70 years. [146-148]

Our study group included 22 (78.6%) males and 6 (21.4%) females. M:F ratio was 3.6:1. The male preponderance in our study was similar to previous studies (Kumar R et al and Siddiqui MA et al) in India and distributions worldwide, giving a male to female ratio as 4:1 [146,150]

HCC surveillance [7-9,] helps to identify early tumors that are amenable to treatment. Indian National Association for Study of the Liver (INASL), advocate a 6-monthly abdominal ultrasonogram for HCC

surveillance[110]. Ultrasound is the most common surveillance and diagnostic imaging technique used in India, owing to its low cost, ease of use and low risk. CT scan is also used and may have more definitions than ultrasound. It is commendable observation that majority of patients in both study group were identified by surveillance, a total of 67.9%.

As documented previously, the primary predisposing condition for HCC in our patients was liver cirrhosis, seen in 18 (64.3%) of patients which was comparable to previous studies which reported 60-70% of incidence.[146]

The most prevalent predisposing condition in our patients was alcoholism 15 (53.65%) and alcohol with viral infection was observed in 5 (17.9%) of our subjects. which was also similar to previous Indian publications. [10, 11, 146-148] It is documented by previous investigators that alcohol alone accounts for approximately 8% of all HCCs and approximately, 9% to 10% have both an alcohol and viral etiology.[148] So our study population showed higher incidence of alcohol as well as combination of viral infection with alcoholism.

Similarly, next predisposing factor observed in our study group was NASH 8 (28.6%). It is reported that about 3%-15% of obese patients with NASH (Non-alcoholic steatohepatitis) develop cirrhosis, whereas about 4%-27% of patients with NASH with cirrhosis acquired HCC.[150] Our observations were hence comparable with previous findings.

The prevalence of HCV documented in our study group was 38.5% in TACE patients and 26.7% in MWA subjects, with a total of 9 (32.1%). The percentage of HBV positivity in our patients was only 1 (3.6%). Kumar R et[146] al reported HBV infection at 73% and evidence of HCV infection in 15% of their patients. The prevalence of HBV positivity in Indian HCC patients ranges between 36-74% %.[10,11, 148] So our study population showed a higher incidence for HCV and a lower incidence for HBV infections.

Antiviral therapy in patients with BCLC-D may improve liver function, expanding the therapeutic window for tumor specific medicines.[8] Because of widespread availability of antiviral medication, the long-

term clinical results in patients with HCV/HBV have improved considerably in recent decades.[158] All our study subjects who had HCV or HBV received antiviral treatment, 5 (38.5%) in TACE and 6 (40.0%) in MWA group.

Hematological and biochemical parameters were comparable with previous publication from India. Majority of our patients were anemic with a mean hemoglobin of 10.8 gm/dL. Hyperbilirubinemia was noted in 53.6% of our patients. Hepatic enzyme disturbances in the form of raised AST, ALT and SAP are seen in 54%, 50% and 32%, respectively, comparable to previous reports of 55%, 39% and 33%.[146-148]

Saini et al evaluated the clinical and biochemical parameters in hepatocellular carcinoma and reported that the normal value of AFP in India is around 10 to 20 ng/mLMean(SD) of AFP values for TACE and MWA group was 150 (20.7) and 80.5 (15.7) respectively. A level greater than 400 ng/mL which is accepted by European Association for Study of Liver (EASL) as diagnostic, is reported to be seen in 46%, but only one patient in our study among TACE group patients had such a value. It is reported that 20 % HCC group have normal value. 6 (46.2%) and 2 (13.3%) among TACE an MWA group had AFP < 20ng/mL.

Staging of hepatocellular carcinoma(HCC) is necessary for guiding prognostication, management, and research purposes that further aid in the improvement of existing clinical and epidemiological health services. The Barcelona Clinic Liver Cancer (BCLC) Staging System[98] is a commonly used tool for guiding HCC treatment strategies both in clinical practice and in clinical trials. In this present study also patient stratification and treatment allocation were based on the Barcelona Clinic Liver Cancer (BCLC) staging system.

Our documented data demonstrated a similar distribution in stages for Child-Pugh (CP) classification, as well as BCLC staging system for HCC, and MELD score among both TACE and MWA study groups.

Total number of lesions treated were 45, 23 lesions in TACE patients and 22 lesions in MWA patients. The maximum number of lesions treated in a single sitting in MWA group was 3. Treating 4 lesions in one sitting was recorded in 2 (15.4%) patients who underwent TACE

procedure. Tumor size in TACE group before treatment ranged from 1.3 x 1.1 cms to 12.1 x 10.14 cms, whereas tumor size in MWA group ranged from 0.8 cms x 0.8 cms to 5.5 x 5.0 cms. Tumor size > 5 cms was recorded in 9 (39.1%) in TACE group vs. 1 (4.5%) in MWA group and tumor size of <2 cms were observed in 4 (17.4%) vs. 10 (45.5%) in TACE and MWA groups, respectively. The tumor size was significantly bigger in TACE group, giving a significance of p=0.015

This observation is expected because of the difference in inclusion criteria for TACE AND MWA.TACE patients selected were in BCLC Stage B; Intermediate stage with large multinodular lesion and Child-Pugh A-B with Performance status 0. And for MWA patients selected were in BCLC Stage 0; Very Early stage with single nodule <2cm in size and Child-Pugh A with Performance status 0, also BCLC Stage A; Early-stage Single or ≤3 nodules ≤ 3 cm in size. Hence the higher number and size of lesion in TACE than MWA.

Majority of lesions treated by LRT were identified as either LI-RADS 5 or LI-RADS 4 prior to the procedure. Six weeks post LRT, 77% TACE patients still had cancer in situ as demonstrated by LR-viable lesion as compared to 7% in MWA group. Also, it was observed that 80% in MWA group had no remaining cancer (LR non-viable) as compared to 15% in TACE group. The difference was highly significant, with p value of 0.001. This observation demonstrated that MWA patients responded better to LTR procedures.

The most widely used tool to evaluate the size of lesions post LRT is the 2010 modified Response Evaluation Criteria in Solid Tumors (mRECIST)[137,138] we have used mRECIST for measuring tumoral response to treatment in our HCC subjects. These systems measure the maximal diameter of the residual tumor (that is, the arterial enhancing portion) in one (mRECIST) or two (EASL) axial dimensions and classify the effect to treatment. as Complete response- No residual area of disease(CR), partial response - 30% decrease in size(PR), (SD) Neither PR nor PD criteria metand progressive disease (PD)- 20% increase in size or new lesion stable disease-

In overall treatment response at 6 weeks as per mRECIST showedno residual lesion (complete response) in 73% of MWA and 15% TACE patients. Partial remission as defined as 30% decrease in size was detected in 15% TACE subjects. Stable disease where HCC persisted was observed in 31% TACE and 7% MWA subjects. Progressive disease defined as 20% increase in size or new lesion was seen in 39% TACE and 13% MWA patients. The observation demonstrated a better prognosis among our MWA patients.

Similarly, the documented survival out-come of our LRT patients 6 months post treatment was as follows. 93% subjects in MWA group were alive compared to 46% among TACE patients. 39% TACE subjects succumbed to the disease compared to 7% in MWA group. 15% patients were lost to follow up in TACE group. The difference observed was significant with a p value 0. 019. This also revealed a better response to treatment among MWA patients.

According to BCLC selection criteria, MWA included early-stage HCC patients (BCLC 0 and A), is the only LRT considered **curative**, being equivalent to surgical resection[20,21]. This could explain the obvious better response to therapy among MWA patients. Transarterial chemoembolization (**TACE**), is considered life prolonging, but ultimately palliative. The BCLC guidelines recommend TACE as the standard first-line treatment for intermediate HCC, BCLC stage B patients.[29]

Golfieri et al[162] in a retrospective review of 271 patients with 635 HCCs treated with TACE analysed lesions that were 2.1–5 cm and found according to mRECIST criteria that after one session of TACE complete response (CR) was seen in 64% and PR in 36% patients. In our study, CR after one session of TACE was 15%, and PR was 15% which is considerably lower than their results.

Lee et al.[163] evaluated 337 patients with HCCs between 3 and 5 cm, 150 of whom underwent TACE and found that overall survival (OS) at 1 years for this cohort of 150 patients was 88.7%. Survival in our TACE group was 46%, 6-month post treatment.

Yin et al[164]investigated the outcome and prognostic factors for percutaneous thermal ablation technique in medium and large

hepatocellular carcinoma and found out that in the patients with 3- to 5-cm HCCs, 80.7% had a CR after an initial intervention. In our study, survival outcome in MWA patients was 93% which was comparable to the above findings.

For a multivariate Cox regression Analysis could not predict an independent risk factor for LRT patients. This could be because of the small number of our cohort.

The outcome in HCC is an interplay between multiple factors including progression of disease, hepatic function etc. Our results are encouraging, MWA giving a CR of 73% with survival outcome of 93% and TACE giving a CR and PR of 15% each and survival outcome of 46%, 6 months post treatment.

We hope that our observations regarding the outcome on LRT treatment for HCC will give an understanding for future planning strategies for the management of HCC using locoregional therapies.

LIMITATIONS

The main limitation of this study is the small study group, which could be attributed to the short period of study and limited follow up. We had also excluded patients who had more than one session of LRT, patients undergoing multimodality treatments and those with changes in treatment protocol during the study period, which would have resulted in incomplete data in additional variables in several patients, as such most patients undergoing treatment by TARE, RFA and PEI had to be excluded from the study.

Strength of our study was that tumor response was re-evaluated by the same radiologists for both treatment groups using uniform criteria.

SUMMARY AND CONCLUSION

Summary:

- The patients included were age and gender matched.
- Basic diagnosis was cirrhosis in majority of patients.
- Child-Pugh (CP) classification, Barcelona Clinic Liver Cancer (BCLC) staging system for HCC, and The Model for End-Stage Liver Disease (MELD) score were comparable in both groups.
- Regarding tumor characteristics, tumor number was comparable in two groups, whereas tumor size was significantly larger among Trans-arterial Chemoembolisation (TACE) group.
- Evaluation of outcome of Locoregional Therapy (LRT) using mRECIST showed significantly superior response to treatment with better survival outcome among MWA patients.

Conclusion: Our observation showed that MWA patients had better prognosis than those who underwent TACE. More studies are required for getting a clearer picture of HCC and experience with locoregional therapy (LRT) in Indian scenario.

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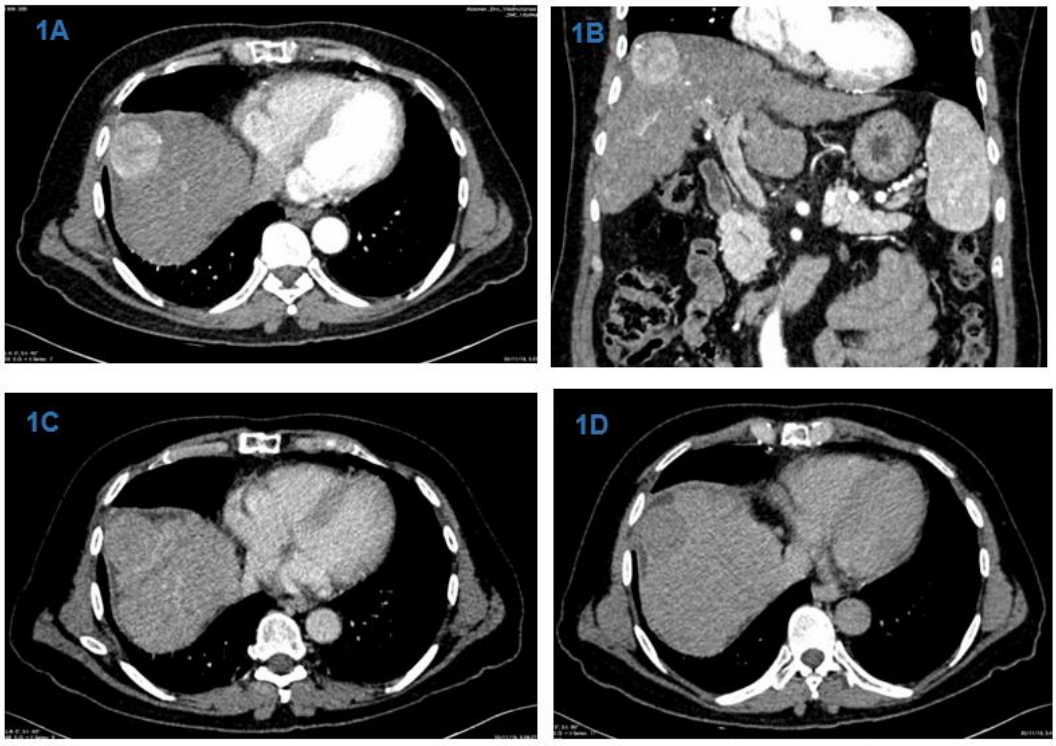
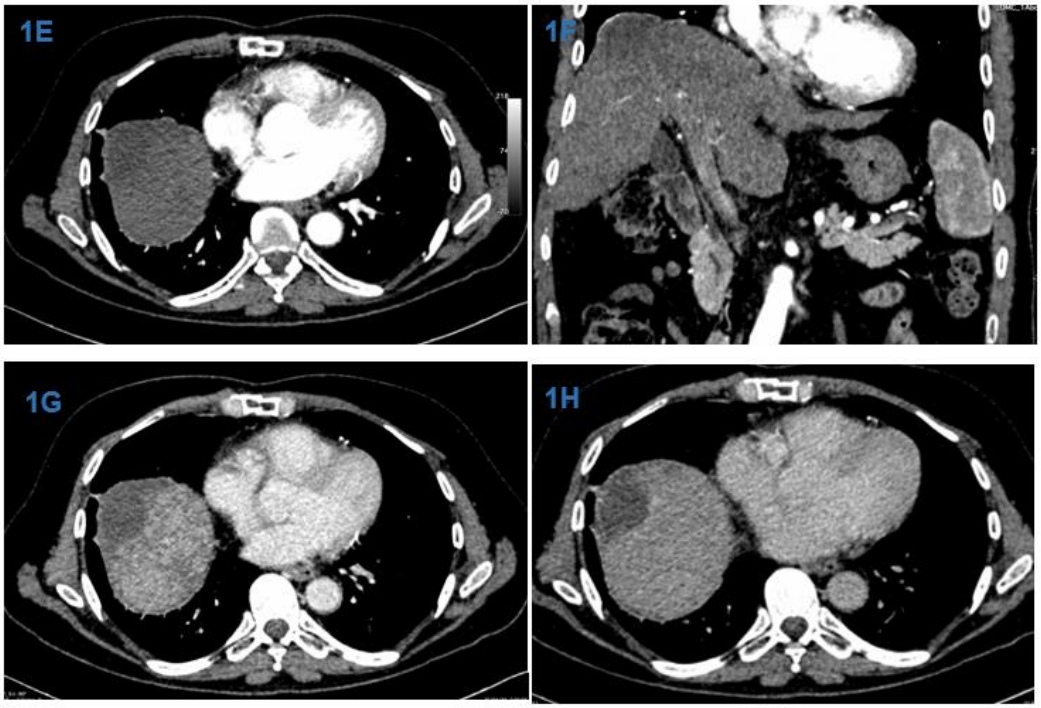


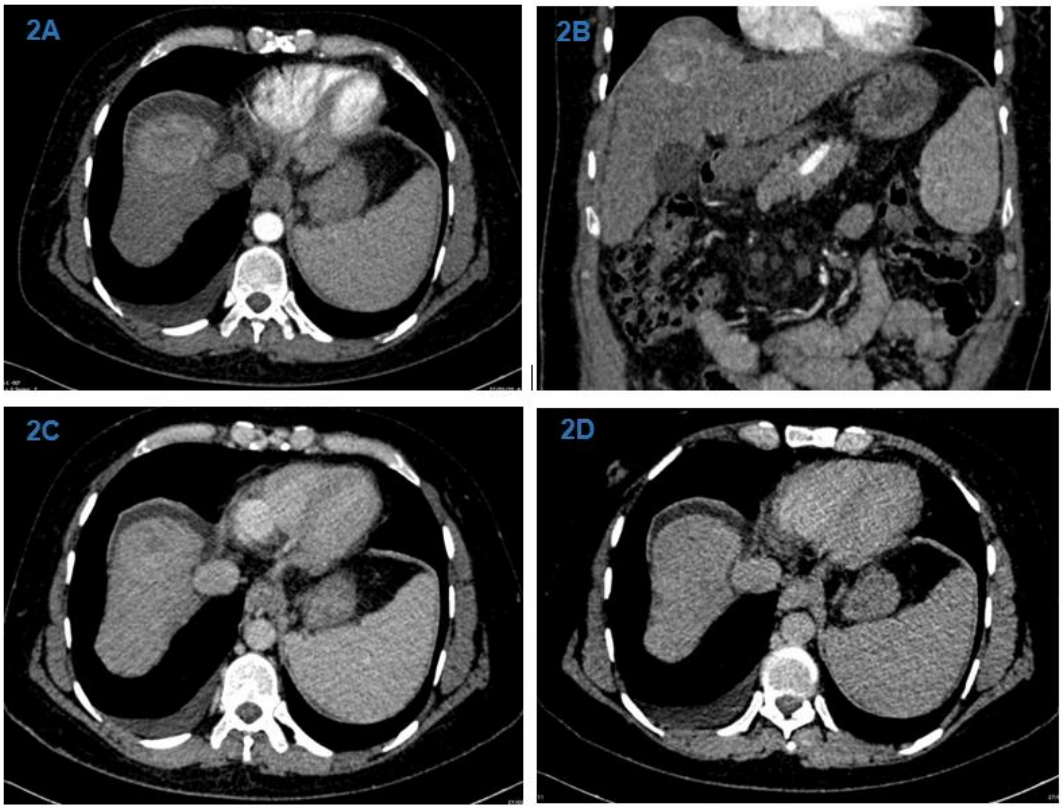
Picture 5a: CASE 1: PATIENT DIAGNOSED CASE OF HCC PLANNED FOR TACE, CT TRIPHASIC IMAGES:

Images 1A and 1B show arterial phase sequences in axial and coronal view respectively, demonstrating an arterially enhancing lesion in segment VIII of liver in subphrenic location bulging exophyticaly and showing washout on delayed phase images. (Images 1C and 1D)



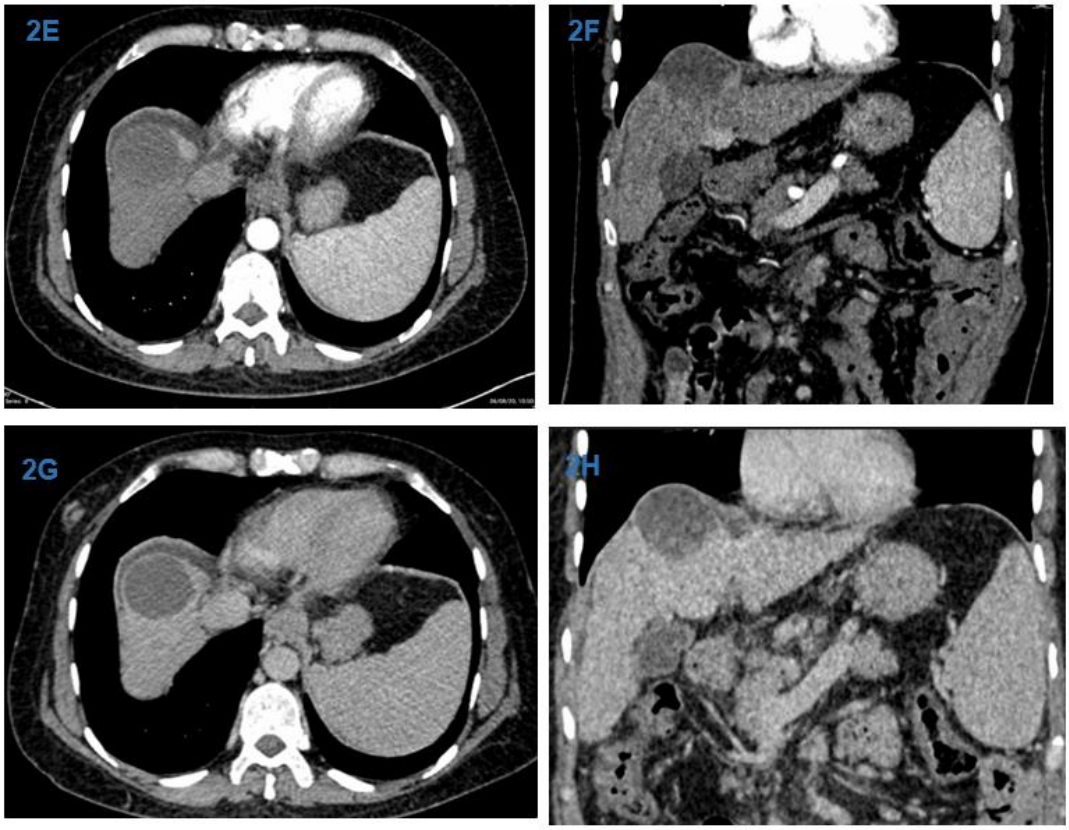
Picture 5b: CASE 1: POST TACE CT TRIPHASIC IMAGING

Post TACE study shows a hypodense area seen in segment VIII of liver in subphrenic location at the site of previously demonstrated lesion with no evidence of any abnormal enhancement on arterial (Images 1E and 1F, axial and coronal view), venous (Image 1G, axial view) or delayed phase (Image 1H, axial view) sequences, representing complete response to therapy.



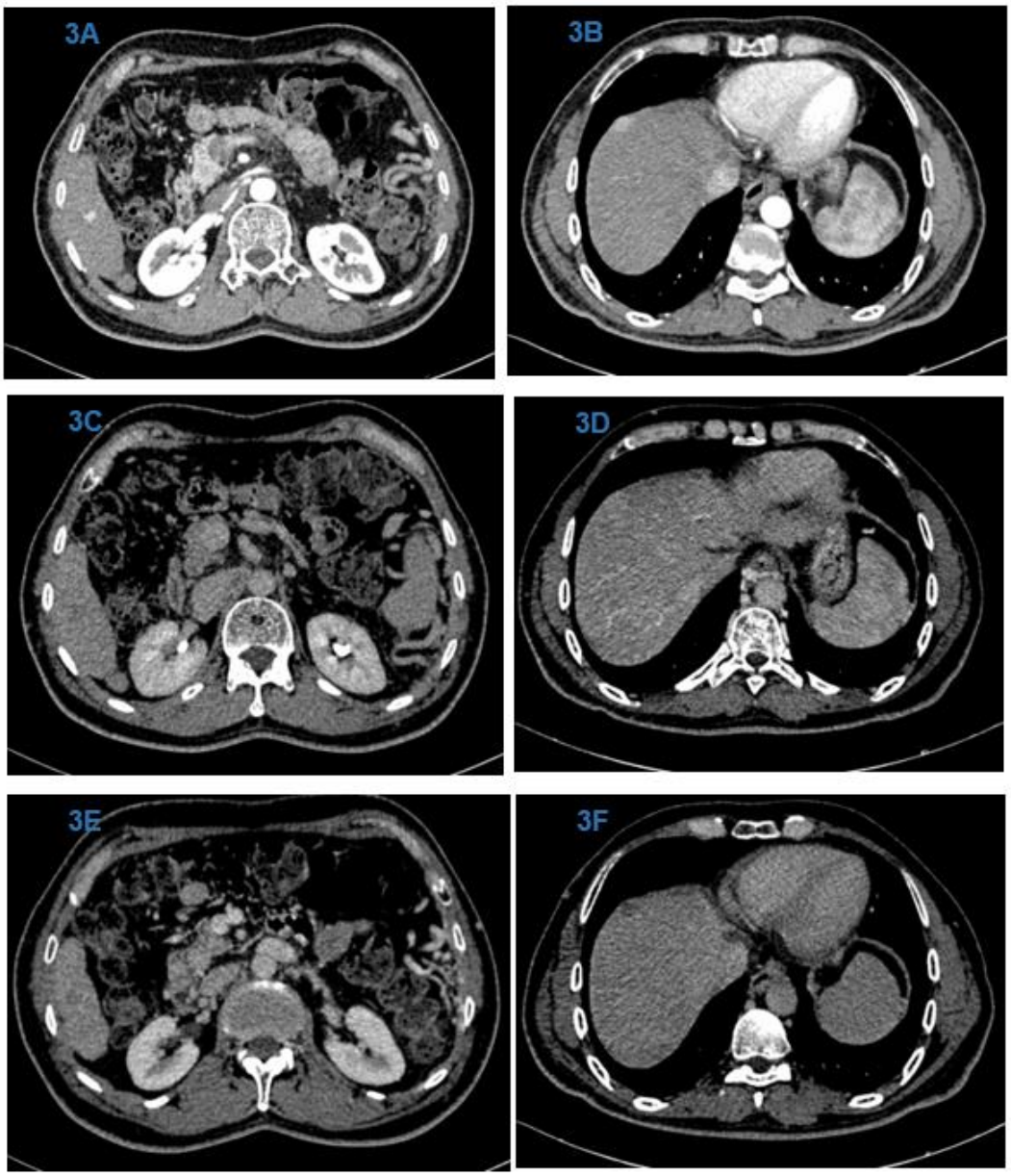
Picture 6a: CASE 2: PATIENT DIAGNOSED CASE OF HCC PLANNED FOR TACE, CT TRIPHASIC IMAGES

Arterial phased sequences (Images 2A and 2B, in axial and coronal view respectively) show a relatively well defined heterogeneously enhancing lesion causing focal contour bulge in segment VIII, showing washout on delayed phase images (Axial Images 2C and 2D respectively) with mild perihepatic fluid.



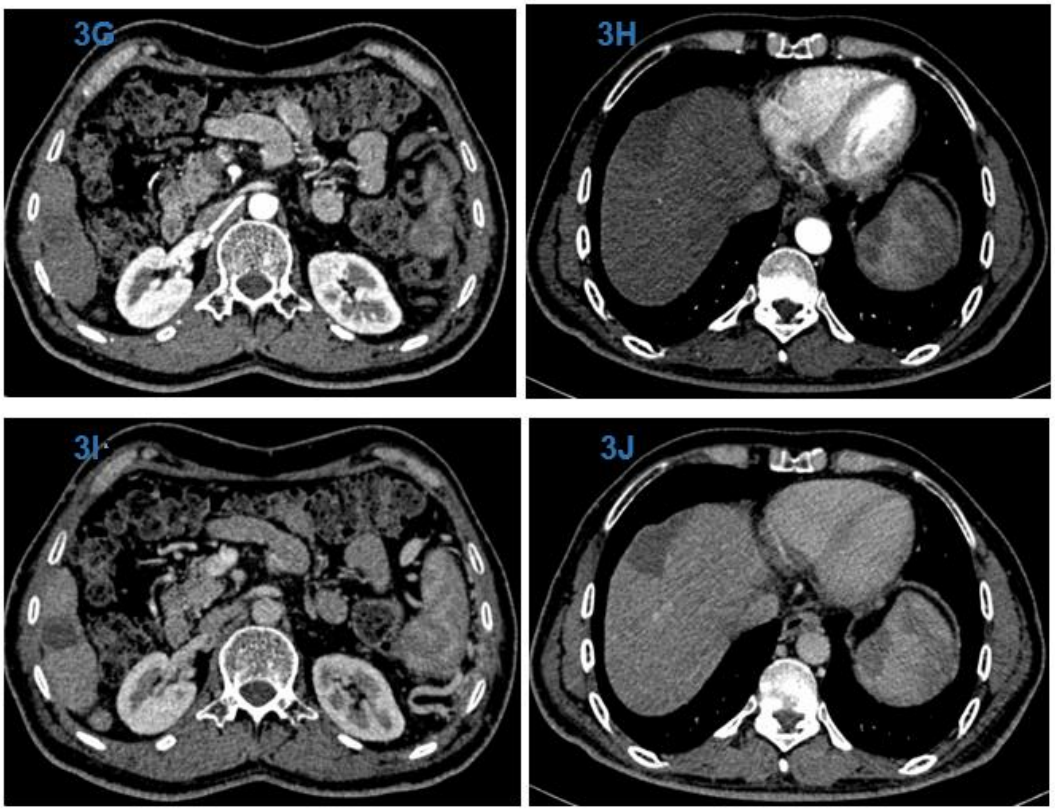
Picture 6b: CASE 2: POST TACE CT TRIPHASIC IMAGING

Post TACE study shows a hypodense post ablation cavity in segment VIII of liver at the site of previously demonstrated lesion with nodular peripherally enhancing area (Images 2E and 2F, axial and coronal view respectively) which shows progressive washout on delayed phase images (Images 2G and 2H, axial and coronal view respectively), Representing partial response to therapy.



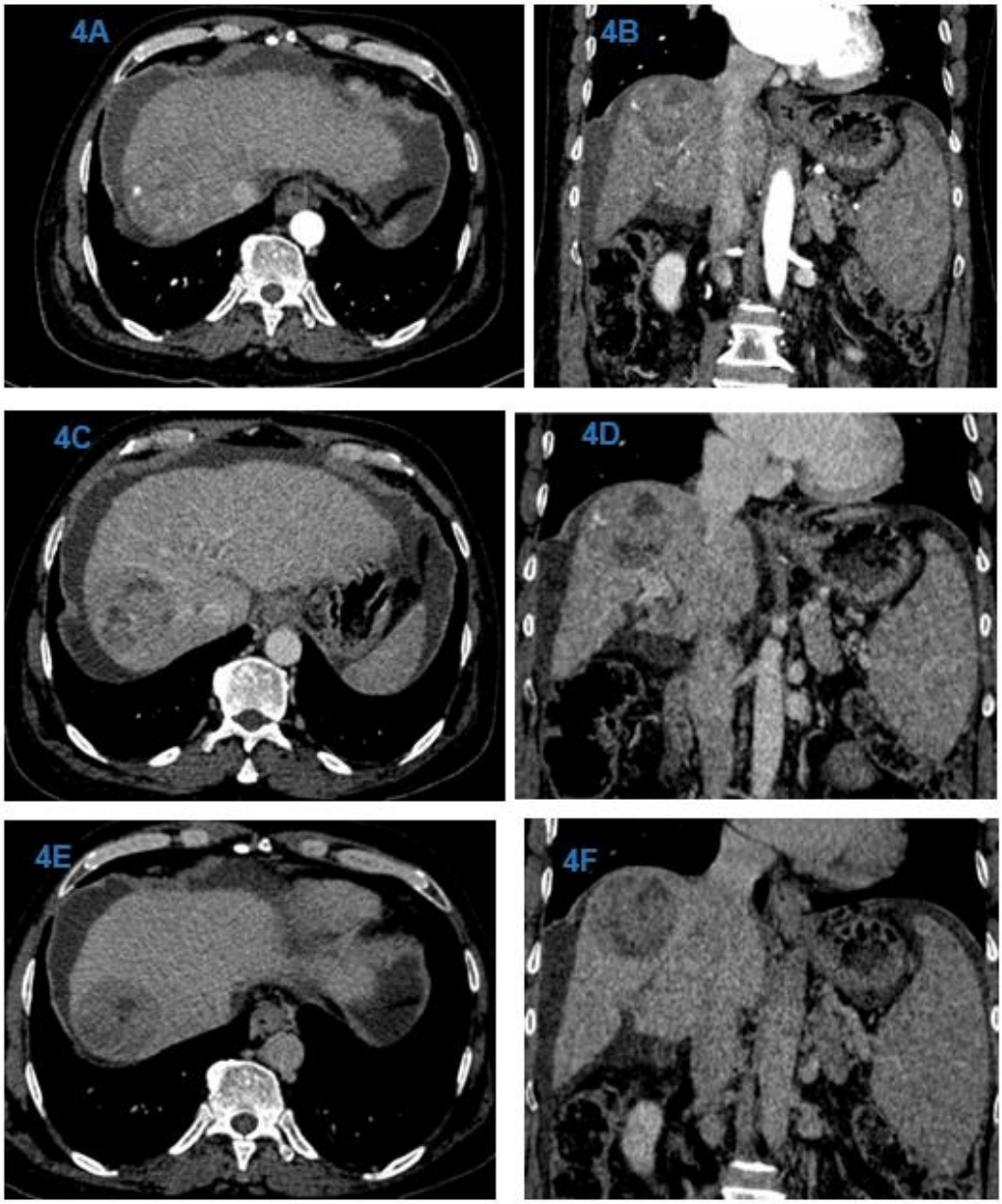
Picture 7a: CASE 3: PATIENT DIAGNOSED CASE OF HCC PLANNED FOR MWA, CT TRIPHASIC AXIAL IMAGES

Images 3A and 3B show an two small relatively well defined arterially enhancing lesions, one seen in segment 2A and 2B arterial phased sequences measuring < 3cm one seen in segement VI of the liver (Image3A) and another in segment VIII in subcapsular location), in venous phase images (3C and 3D) and delayed phase images (3E and 3F) they show progressive washout.



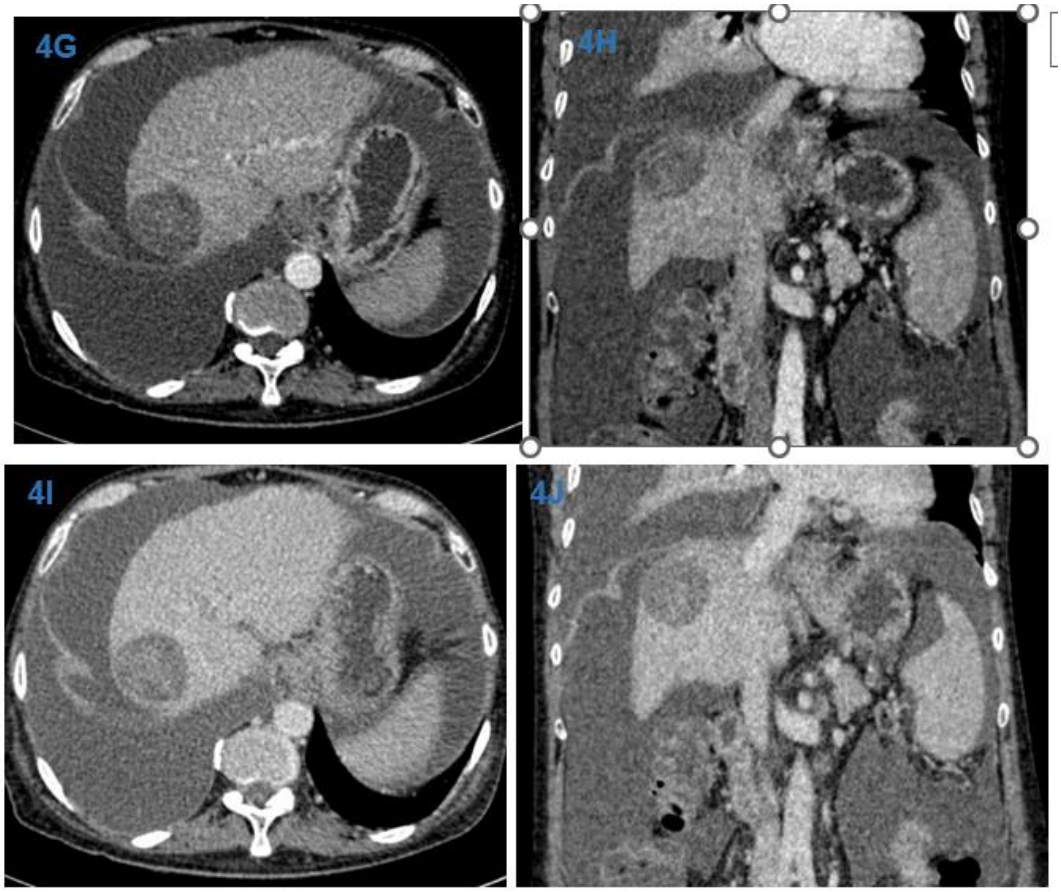
Picture 7b: CASE 3: POST MWA CT TRIPHASIC IMAGING

Post MWA CT triphasic study shows two well defined hypodense post ablation cavities seen in segment VI and VIII of liver at the site of previously demonstrated lesions with no evidence of any abnormal enhancement in arterial phase (Images 3G and 3H) venous phase (Images 3I and 3J), representing complete response



Picture 8a: CASE 4: PATIENT DIAGNOSED CASE OF HCC PLANNED FOR MWA, CT TRIPHASIC IMAGES

Images 4A and 4B show a heterogeneously iso-hypodense lesion in segment VII/VIII of the right lobe of liver, showing patchy arterial enhancement and increased neovascularity (Images 4A and 4B, axial and coronal view respectively) and showing progressive washout on venous phase images (Images 4C and 4D, axial and coronal view respectively) and delayed phase images (Images 4E and 4F, axial and coronal view respectively



Picture 8b: CASE 4: POST MWA CT TRIPHASIC IMAGING

Post MWA CT triphasic study shows a well defined hypodense non enhancing lesion in segment VII/VIII at the site of previously demonstrated lesion representing the post ablation cavity with small amount of hyperdense content seen within it and showing no abnormal enhancement on arterial phase images (Images 4G and 4H, axial and coronal views respectively) and on venous phase images (Images 4I and 4J, axial and coronal views respectively), representing complete response.

S.No	MRD	INITIALS	AGE SEX	SEX	NO.OF LESIONS	LESION 1												
-	-	-	-	-	-	SEGMENT	SIZE (cm)	APHE	PORTAL	VENOUS	LIRADS	MWA ZONE (cm)	MWA TIME	POWER	SEGMENT	SIZE (cm)	APHE	PORTAL
1	1188711	NS	65	M	1	VI	5.0 X 5.0	YES	WASHOUT	WASHOUT	V	5.5 X 5.4	15 MIN	100W	0	0	0	0
2	29233	KK	55	F	1	VIII	1.1 X 1.3	YES	WASHOUT	WASHOUT	V	3.4 X 2.9	2 MIN	100W	0	0	0	0
3	428361	GS	56	M	2	VIII	1.5 X 1.2	YES	WASHOUT	WASHOUT	V	3.4 X 2.9	2 MIN	100W	VI	0.8 X 0.8	YES	WASHOUT
4	1138000	ND	66	F	1	VI	3.0 X 2.8	YES	WASHOUT	WASHOUT	V	3.5 x 3.2	5 MIN	100W	0	0	0	0
5	50336	GK	66	F	1	IV B	1.3 X 1.3	YES	WASHOUT	WASHOUT	V	3.1 X 3.7	3 MIN	100W	0	0	0	0
6	1140560	DS	53	M	1	VII	4.9 X 4.8	YES	WASHOUT	WASHOUT	V	5.5 X 5.4	15 MIN	100W	0	0	0	0
7	234553	CL	71	M	1	II/III	3.4 X 3.1	YES	WASHOUT	WASHOUT	V	4.5 X 3.9	13MIN	100W	0	0	0	0
8	940257	VPD	72	M	3	VI	3.2 X 3.0	YES	WASHOUT	WASHOUT	V	4.5 X 3.9	13 MIN	100W	II	2.3 X 2.0	YES	NO
9	1162884	BS	63	M	1	VIII	4.0 X 3.8	YES	WASHOUT	WASHOUT	V	4.5 X 3.9	13 MIN	100W	0	0	0	0
10	1145734	RK	62	M	3	VI/VII	1.7 X 1.4	YES	WASHOUT	WASHOUT	V	3.1 X 3.7	3 MIN	100W	VIII	3.1 X 2.4	YES	WASHOUT
11	1236781	AS	46	M	2	I	2.0 X 1.7	YES	WASHOUT	WASHOUT	V	3.4 X 2.9	2 MIN	100W	VI	1.3 X 0.8	YES	WASHOUT
12	217864	RK	63	M	1	VIII	4.9 X 4.7	YES	WASHOUT	WASHOUT	V	5.5 X 5.4	15 MIN	100W	0	0	0	0
13	1076314	SRG	81	F	1	IV	5.0 X 4.8	YES	WASHOUT	WASHOUT	V	5.5 X 5.4	15 MIN	100W	0	0	0	0
14	966261	GR	60	M	1	VII	1.6 X 1.6	YES	WASHOUT	WASHOUT	V	2.9 X 3.4	2 MIN	100W	0	0	0	0
15	334842	SS	54	M	2	VIII	2.3 X 2.0	YES	WASHOUT	WASHOUT	V	3.7 X 3.5	5 MIN	100W	0	0	0	0

S.No	MRD	INITIALS	LESION 2					LESION 3									LES
-	-	-	VENOUS	LIRADS	MWA ZONE (cm)	MWA TIME	POWER	SEGMENT	SIZE (cm)	APHE	PORTAL	VENOUS	LIRADS	MWA ZONE (cm)	MWA TIME	POWER	LR-TR 6 Wks
1	1188711	NS	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	29233	KK	0	0	0	0	0	0	0	0	0	0	0	0	0	0	LR-TR VIABLE
3	428361	GS	WASHOUT	IV	2.3 X 2.8	1 MIN	100W	0	0	0	0	0	0	0	0	0	LR-TR EQUIVOCAL
4	1138000	ND	0	0	0	0	0	0	0	0	0	0	0	0	0	0	LR-TR NON VIABLE
5	50336	GK	0	0	0	0	0	0	0	0	0	0	0	0	0	0	LR-TR NON VIABLE
6	1140560	DS	0	0	0	0	0	0	0	0	0	0	0	0	0	0	LR-TR NON VIABLE
7	234553	CL	0	0	0	0	0	0	0	0	0	0	0	0	0	0	LR-TR NONVIABLE
8	940257	VPD	NO	IV	3.9 X 3.4	5 MIN	100W	VI	1.5 X 1.2	YES	WASHOUT	WASHOUT	V	2.8 X 2.3	1MIN	100 W	LR-TR NONVIABLE
9	1162884	BS	0	0	0	0	0	0	0	0	0	0	0	0	0	0	LR-TR NONVIABLE
10	1145734	RK	WASHOUT	V	4.5 X 3.9	13MIN	100W	VIII	1.3 X 1.3	YES	WASHOUT	WASHOUT	V	3.4 X 2.9	2 MIN	100W	LR-TR NONVIABLE
11	1236781	AS	WASHOUT	V	2.3 X 2.8	1 MIN	100W	0	0	0	0	0	0	0	0	0	LT-TR NONVIABLE
12	217864	RK	0	0	0	0	0	0	0	0	0	0	0	0	0	0	LT-TR NONVIABLE
13	1076314	SRG	0	0	0	0	0	0	0	0	0	0	0	0	0	0	LR-TR NONVIABLE
14	966261	GR	0	0	0	0	0	0	0	0	0	0	0	0	0	0	LR-TR NONVIABLE
15	334842	SS	0	0	0	0	0	0	0	0	0	0	0	0	0	0	LR-TR NONVIABLE

S.No	MRD	INITIALS	ON 1	LESION 2		LESION 3			mRECIST	-	COMPLICATION
-	-	-	LR-TR 3 months	LR-TR 6 Wks	LR-TR 3 mnth	LR-TR 6 Wks	LR-TR 3 mnth		at 6weeks	at 3 months	
1	1188711	NS	0	0	0	0	0	bleed in post-ablation cavity	0	0	DEATH
2	29233	KK	LR-TR VIABLE	0	0	0	0	2 new lesions at 6 weeks	PD	PD	-
3	428361	GS	LR-TR NONVIABLE	LR-TR NONVIABLE	LR-TR NONVIABLE	0	0	-	CR	CR	-
4	1138000	ND	LR-TR NONVIABLE	0	0	0	0	-	CR	CR	-
5	50336	GK	LR-TR NONVIABLE	0	0	0	0	-	CR	CR	-
6	1140560	DS	LR-TR NONVIABLE	0	0	0	0	-	CR	CR	-
7	234553	CL	LR-TR NONVIABLE	0	0	0	0	-	CR	CR	-
8	940257	VPD	LR-TR NONVIABLE	LR-TR VIABLE	LR-TR VIABLE	LR-TR VIABLE	LR-TR VIABLE	-	SD	SD	-
9	1162884	BS	LR-TR NONVIABLE	0	0	0	0	-	CR	CR	-
10	1145734	RK	LR-TR NONVIABLE	LR-TR NONVIABLE	LR-TR NONVIABLE	LR-TR NONVIABLE	LR-TR NONVIABLE	-	CR	CR	-
11	1236781	AS	LR-TR NONVIABLE	LR-TR NONVIABLE	LR-TR NONVIABLE	0	0	new lesion in seg VIII at 6 weeks and multiple at 3 months	PD	PD	-
12	217864	RK	LT-TR NONVIABLE	0	0	0	0	-	CR	CR	-
13	1076314	SRG	LT-TR NONVIABLE	0	0	0	0	-	CR	CR	-
14	966261	GR	LR-TR NONVIABLE	0	0	0	0	one new lesion at 3 months	CR	PD	-
15	334842	SS	LR-TR NONVIABLE	0	0	0	0	one new lesion at 3 months	CR	PD	-

									BEFORE RX	CT ABD								LESION2								LESION 3			
TACE1. MWA.2	S. No	Intials	Age	Sex	MRD	SOL	TOTAL NO.OF LESIONS	COUINAUD SEGMENT	NO OF LESION SEGMENT	COUINAUD. SEGMENT	LR	SIZE	APHE	PORTAL	VENOUS	DELAYED PHASE	FNAC/BX	NO OF LESION	COUINAUD. SEGMENT	LR	SIZE	APHE	PORTAL	VENOUS	FNAC/BX	NO OF LESION	COUINAUD. SEGMENT	LR	SIZE
1	1	BS	55	M	858846	YES	3	VIII,III, VIII	1	VIII	LR-5	4.1X3.5CM	YES	-	WASHOUT	WASHOUT	HCC	1	III, L LOBE	LR-5	1.3X1.1CM	YES	WASHOUT	WASHOUT	-	2	VIII	LR-3	6MM
1	2	PS	52	M	763086	YES	1	V,VI. VIII	1	V,VI,VIII	LR-5	LARGE,MULTIPLE LOBULATED NODULES	YES	-	WASHOUT	WASH OUT	NO	0	0	0	0	O	0	0	0	0	0	0	0
1	3	HS	65	M	860820	YES	1	V/VIII	1	V/VIII	LR-5	6.7X6.6CM	YES	-	WASHOUT	WASH OUT	NO	0	0	0	0	0	0	0	0	0	0	0	0
1	4	SD	51	M	392419	INFILTRATIVE HCC, TUMOR IN VEIN	1	VII, VI	1	VI&VII	LR-TIV	12.1X6.2X10.4 CM	YES	-	WASHOUT	WASH OUT	NO	0	0	0	0	0	0	0	0	0	0	0	0
1	5	SP	57	M	1322924	YES	1	VII/VI	1	VII/VI	LR-5	6.9X5.8X7 CM	YES	-	WASHOUT	WASH OUT	-	0	0	0	0	0	0	0	0	0	0	0	0
1	6	SVS	84	M	1324104	YES	1	VIII,V.I	1	VIII/V	LR-5	8X7.6X8.3 CM	YES	-	WASHOUT	WASH OUT	-	0	0	0	0	0	0	0	0	0	0	0	0
1	7	BS	58	M	1286987	YES	3	II,VIII/V,VI	1	II	LR-5	7X3.5X3.4CM	YES	-	WASHOUT	WASH OUT	-	1	VIII/V	LR-5	5.2X2.7CM	YES	WASHOUT	WASHOUT	-	1	VI	LR-5	2.1X1.8CM
1	8	MRM	64	F	1097131	YES	4	VI,V/VIII,IVa	1	VI	LR-5	5.6X7 CM	YES	-	WASHOUT	WASH OUT	-	1	VIII/V	LR-5	2.9X2.5CM	YES	WASHOUT	WASHOUT	-	1	IVa	LR-5	1.0X1.0 CM
1	9	AK	50	F	641416	YES	1	VI	1	VI	LR-5	5.5X3.3X5.0 CM	YES	-	WASHOUT	WASH OUT	-	0	0	0	0	0	0	0	0	0	0	0	0
1	10	AK	55	M	869663	YES	3	VI,IV,VII	1	VI	LR-5	4.1X2.8CM	YES	-	WASHOUT	WASH OUT	-	1	IV	LR-5	1.7X1.4CM	YES	WASHOUT	WASHOUT	-	1	VII	LR-5	1.3CM
1	11	RK	51	M	546458	YES	1	VIII	1	VIII	LR-5	5.3X5.3CM	YES	-	WASHOUT	WASH OUT	-	0	0	0	0	0	0	0	0	0	0	0	0
1	12	DJ	66	M	407857	YES	2	VI,VIII	1	VI	LR-5	3.7X3.0 CM	YES	-	WASHOUT	WASH OUT	-	1	VIII	LR-3	-	-	-	-	-	0	0	0	0
1	13	VKJ	59	M	924473	YES, TIV	2	VII,II	1	VII	LR-5	2.8X2.6CM	YES	-	WASHOUT	WASH OUT	-	1	II	LR-4	1.7X1.5CM	YES	NO	NO	-	0	0	0	0

							LESION 1	FOLLOW UP,6 W	LESION 2		LESION 3		F/U-3M-LESION 1	LESION2	LESION 3	F/U-1YR,LESION1	LESION 2	LESION 3	MRECIST	MRECIST,	MRECIST	SURVIVAL	F/U,MONTHS	CAUSE OF DEATH
TACE1. MWA.2	S. No	Intials	APHE	PORTAL	VENOUS	FNAC/BX	LR	SIZE	LR	SIZE	-	LR	LR	LR	-	0	0	0	6WEEKS	3MONTHS	1YR	-	-	-
1	1	BS	YES	NO WASH OUT	NO WASH OUT	-	LR-5 LR-TRV(VIABLE-SEG VIII)	1.2X0.7 CM	LR -4	.8X.7	0	-	LR-NV	LR-III	NOT SEEN	2.9X2.2,SEGM VIII LR-VIABLE	3.4X1.8,LR-5	13MM,SEG III,LR-5	PR	CR	PD	LOST F/U	24	-
1	2	PS	0	0	0	-	LR-TRV(VIABLE)	LARGE	0	0	0	0	0	0	0	0	0	0	PD	PD	0	DEATH	<6M0NTHS	DECOMPENSATED CIRRHOSIS
1	3	HS	0	0	0	-	LR-4(SEG V/VIII)	10X8MM	LR-5(SEG VII) NEW LESION	11X8MM	3LESIONS , L LOBE	LR-3, 14X11 MM	0	0	0	0	0	0	PD	PD	0	YES	>6M	-
1	4	SD	0	0	0	-	LRTR-NON VIABLE	-	-	-	-	-	0	0	-	LR-TR-NON VIABLE	0	0	CR	CR	CR	YES	12	-
1	5	SP	0	0	0	-	LRTR-VIABLE	6.3X6.1X6.8	-	-	-	-	0	0	-	0	0	0	SD	SD	SD	YES	12	-
1	6	SVS	0	0	0	-	LRTR-VIABLE	-	-	-	-	-	0	0	-	0	0	0	SD	SD	0	YES	>6M	-
1	7	BS	YES	WASH OUT	WASH OUT	-	LRTR-NON VIABLE(SEGII	6X5CM	LRTR-NON VIABLE(SEG VII	-	1X7CM	LRTR-NON VIABLE(SEGV II	0	0	-	0	0	0	CR	CR	CR	YES	>1YR	-
1	8	MRM	YES	WASH OUT	WASH OUT	IVa, NEW	LRTR-VIABLE(SEG V)	4.9X4.7CM	V/VIII LRTR-VIABLE	3.3X3.5CM	IVa , 1.0X1.0	LRTR-VIABLE(SEG IVa)	0	0	-	0	0	0	PD	PD	0	DEATH	6M	DECOMPENSATED CIRRHOSIS
1	9	AK	0	0	0	-	LRTR-VIABLE(SEG VI)	2.4x3.2 CM	-	-	-	-	0	0	-	0	0	0	SD	SD	0	LOST F/U	6M	-
1	10	AK	YES	WASH OUT	WASH OUT	-	LRTR VIABLE(SEG VI)	2.5X2.3	IVa, LR-VIABLE, LR-5	2.3X2.1CM	VII,1.3CM	LR-5	0	0	-	VIII, LR TR VIABLE, NEW LESION LR-5(SEG II)	0	0	SD	SD	0	DEATH	<6M	DECOMPENSATED CIRRHOSIS
1	11	RK	0	0	0	-	LRTR VIABLE(SEG VIII)	2.6X1.3CM	-	-	-	-	0	0	-	0	0	0	PR	PD	PD	YES	> 1 YR	-
1	12	DJ	0	0	0	-	LR-5> SIZE,(SEG VI	4.5X4.1	-	-	-	-	LR-VIABLE	NEW MULTIPLE LESIONS RT LOBE	-	0	0	0	PD	PD	0	DEATH	6M	DECOMPENSATED CIRRHOSIS
1	13	VKJ	0	0	0	-	-	-	-	-	-	-	0	0	-	0	0	0	PD	PD	0	DEATH	6M	DECOMPENSATED CIRRHOSIS

TACE1/MWA.2	S.No	MRD	Initials	Age	Sex	BASIC DIAGNOSIS	IF CIRRHOSIS: RISK FACTORS	ASCITIS	ENCEPHALOPATHY	VIRAL LOAD	ANTI.VIRAL RX	VIRAL STATUS	ALCOHOL	SMOKER	OPIUM	PRESENTATION	FH. CIRRHOSIS	T. BILIRUBIN	D. BILIRUBIN	IND. BILIRUBIN
1	1	858846	BS	55	M	CLD	HCV, ALCOHOL	YES,MILD	NO	NO	COMPLETED	ABSENT	YES	NO	YES	SURVEILLANCE	NO	0.42	0.29	0.13
1	2	763086	PS	52	M	CIRRHOSIS	HCV, ALCOHOL	NO	NO	NO	COMPLETED	ABSENT	YES	YES	NO	SURVEILLANCE	NO	0.72	0.23	0.49
1	3	860820	HS	65	M	CIRRHOSIS	HCV, ALCOHOL	YES, SIGNIFICANT	NO	NO	ON TREATMENT	ABSENT	YES	NO	YES	INCIDENTAL	NO	1	0.35	0.65
1	4	392419	SD	51	M	CLD	NASH	NO	NO	NO	NIL	ABSENT	NO	NO	NO	SURVEILLANCE	NO	9.1	5.4	3.7
1	5	1322924	SP	57	M	CIRRHOSIS	NASH	YES,MILD	NO	NO	NIL	ABSENT	NO	NO	NO	SURVEILLANCE	NO	1.1	0.5	0.6
1	6	1324104	SVS	84	M	CLD	NASH	YES, MODERATE	NO	NO	NIL	ABSENT	NO	NO	NO	INCIDENTAL	NO	1.5	0.9	0.6
1	7	1286987	BS	58	M	CLD	ALCOHOL	NO	NO	NO	NIL	ABSENT	YES	NO	NO	SURVEILLANCE	NO	1	0.3	0.7
1	8	1097131	MRM	64	F	CIRRHOSIS	ALCOHOL	YES,MILD	NO	NO	NIL	ABSENT	YES	NO	NO	SURVEILLANCE	NO	0.6	0.1	0.5
1	9	641416	AK	50	F	CLD	NASH	NO	NO	NO	NIL	ABSENT	NO	NO	NO	INCIDENTAL	NO	0.3	0.12	0.5
1	10	869663	AK	55	M	CIRRHOSIS	ALCOHOL	NO	NO	NO	NIL	ABSENT	YES	NO	NO	SURVEILLANCE	NO	2.2	1.3	0.9
1	11	546458	RK	51	M	CIRRHOSIS	HCV	YES,MILD	NO	NO	COMPLETED	ABSENT	NO	YES	YES	SURVEILLANCE	NO	0.9	0.5	0.4
1	12	407857	DJ	66	M	CLD	NASH	YES,MILD	YES,GR II, RESOLVED BEFORE TACE	NO	NIL	ABSENT	NO	NO	NO	SURVEILLANCE	NO	1.5	0.4	1.1
1	13	924473	VKJ	59	M	CIRRHOSIS	HCV	YES, SIGNIFICANT, LARGE	NO	NO	COMPLETED	ABSENT	YES	NO	YES	SURVEILLANCE	NO	1.1	0.5	0.6
2	1	1188711	NS	65	M	CIRRHOSIS	HCV, ALCOHOL	YES	NO	NO	COMPLETED	ABSENT	YES	NO	NO	SURVEILLANCE	NO	0.67	0.23	0.5
2	2	29233	KK	55	F	CLD	NASH	NO	NO	NO	NIL	ABSENT	NO	NO	NO	SURVEILLANCE	NO	1.68	0.8	0.5
2	3	428361	GS	56	M	CIRRHOSIS	HCV	NO	NO	NO	ON TREATMENT	ABSENT	NO	NO	NO	SURVEILLANCE	NO	0.8	0.39	0.9
2	4	1138000	ND	66	F	CLD	NASH	YES	NO	NO	NIL	ABSENT	NO	NO	NO	SURVEILLANCE	NO	0.45	0.22	0.4
2	5	50336	GK	66	F	CLD	HCV	NO	NO	NO	ON TREATMENT	ABSENT	NO	NO	NO	INCIDENTAL	NO	2	0.5	1.1
2	6	1140560	DS	53	M	CIRRHOSIS	ALCOHOL	YES	NO	NO	NIL	ABSENT	YES	YES	YES	SURVEILLANCE	NO	1.9	1	0.6
2	7	234553	CL	71	M	CIRRHOSIS	HBV, ALCOHOL	NO	NO	NO	COMPLETED	ABSENT	YES	YES	NO	SURVEILLANCE	NO	0.46	0.2	3.7
2	8	940257	VPD	72	M	CIRRHOSIS	ALCOHOL	YES	NO	NO	NIL	ABSENT	YES	YES	NO	INCIDENTAL	NO	1.5	1.03	0.6

TACE1/MWA.2	S.No	MRD	SGOT	SGPT	T. ALBUMIN	T. PROTEIN	ALK PHOS	HB	WBC	PLT	PT/INR	S. CREAT	S. UREA	AFP.	CHILD-PUGH	MELD	BCLC	L LOBE HYPERTROPHY	VASCULAR THROMBOSIS	METASTASIS	ANY COLLATERAL	TOTAL NO.OF LESIONS BEFORE RX	COUINAUD SEGMENTS-FOR LESIONS BEFORE RX	NO OF LESION
1	1	858846	157	116	6.5	3.3	103	12	2.6	70	1.3	0.73	14	64	CLASS B	9	STAGE B	YES	NO	NO	L GASTRIC,SPLENORENAL	4	VIII,III, VIII	1
1	2	763086	141	222	3.3	7.8	222	12	6	231	1.1	0.93	31	166	CLASS B	7	STAGE B	YES	NO	VERTEBRAL	NO	1	V,VI, VIII	1
1	3	860820	125	37	3.2	7	92	10	4.9	174	1.4	0.67	17	196	CLASS B	10	STAGE B	NO	NO	NO	L GASTRIC,SHORT GASTRIC, POST GASTRIC,SPLENO-RENAL	1	V/VIII	1
1	4	392419	191	203	1.9	5.7	376	9.3	7.8	208	1.36	1.08	63	>3000	CLASS B	19	STAGE B	YES	PV, RT BRANCH	NO	L GASTRIC, SPLENO-RENAL	1	VII, VI	1
1	5	1322924	19	13	9.2	7.1	89	8.9	1	20	1.4	0.93	21	366	CLASS A	11	STAGE-B	NO	MAIN PV,SPLENIC VEIN	NO	NO	1	VII/VI	1
1	6	1324104	93	69	2.8	6.4	391	12	4.5	128	1.3	0.73	30	234	CLASS A	11	STAGE A	NO	NO	NO	NO	1	VIII,V,I	1
1	7	1286987	43	40	4.2	6.6	69	13	4.7	81	1.3	0.6	7	-	CLASS A	9	STAGE A	NO	NO	NO	NO	3	II,VIII/V,VI	1
1	8	1097131	38	41	3.3	6.2	264	12	51	288	1.3	1.1	44	-	CLASS A	11	STAGE B	YES	NO	NO	SHORT GASTRIC, SPLENO-RENAL	4	VI,V/VIII,IVa	1
1	9	641416	32	27	3.5	5.8	50	6.9	1.8	100	1.3	0.83	42	8.4	CLASS A	9	STAGE A	NO	NO	NO	PERI GASTRIC, SPLENIC HILUM	1	VI	1
1	10	869663	52	35	3.3	7.4	203	11	3.7	190	1.4	0.7	15	17.7	CLASS B	15	STAGE A	NO	NO	NO	NO	3	VI,IV,VII	1
1	11	546458	34	20	3.6	6.7	90	11	9.3	70	1.4	0.6	15	-	CLASS A	11	STAGE B	NO	NO	NO	NO	1	VIII	1
1	12	407857	90	32	3	7.1	89	8.1	4.2	150	1.7	0.8	28	-	CLASS B	14	STAGE B	YES	NO	NO	NO	1	VI,	1
1	13	924473	33	29	3.9	68	70	14	3	60	1.1	0.7	22	-	CLASS B	8	STAGE B	NO	YES, RT HEPATIC VEIN	YES, PUL NODULE	NO	1	VII,	1
2	1	1188711	38	53	3.7	7.6	95	5.2	10	250	1.08	1.65	86	4.27	CLASS B	12	STAGE B	YES	NO	NO	NO	1	`VI	1
2	2	29233	40	18	3.8	7.3	400	9.1	1.8	46	1.5	0.89	29	.	CLASS B	13	STAGE O	NO	NO	NO	NO	1	VIII	1
2	3	428361	75	66	4.15	7.1	72	13	3.5	50	1.06	0.71	24	.	CLASS A	7	STAGE A	NO	NO	NO	NO	2	VIII,VI	1
2	4	1138000	42	38	3.6	6.5	264	13	4.1	60	1.18	0.24	18	267	CLASS A	8	STAGE A	NO	NO	NO	NO	1	VI	1
2	5	50336	212	97	2.89	5.4	60	12	5.1	154	1.31	0.39	28	6.47	CLASS B	12	STAGE A	NO	NO	NO	NO	1	IV B	1
2	6	1140560	92	57	2	5.8	203	9.9	6.2	90	1.98	0.53	22	2.62	CLASS B	20	STAGE B	YES	NO	NO	NO	1	VII	1
2	7	234553	31	17	4.3	7.3	100	12	5.7	156	1.17	0.88	24	.	CLASS A	8	STAGE B	YES	NO	NO	NO	1	II/III	1
2	8	940257	25	11	3.1	6.3	230	10	3.3	70	1.4	0.78	19	.	CLASS B	14	STAGE B	YES	NO	NO	NO	3	VI,II,VI	1

			BEFORE TREATMENT(BLUE COLOR LESION1,YELLOW COLOR LESION 2, GREEN COLOR LESION 3)																
TACE1/MWA.2	S.No	MRD	LESION 1-COUINAUD. SEGMENT	LESION 1-LR	LESION 1-SIZE, CM	LESION 1-APHE	LESION 1-PORTAL	LESION 1-VENOUS	LESION 1-DELAYED PHASE	LESION 1-FNAC/BX	LESION 2-NO OF LESION	LESION 2-COUINAUD.SEGMENT	LESION 2-LR	LESION 2-SIZE, CM	LESION 2-APHE	LESION 2-PORTAL	LESION 2-VENOUS	LESION 3-NO OF LESION	LESION 3-COUINAUD.SEGMENT
1	1	858846	VIII	LR-5	4.1X3.5	YES	-	WASHOUT	WASHOUT	HCC	1	III, L LOBE	LR-5	1.3X1.1CM	YES	WASHOUT	WASHOUT	2	VIII
1	2	763086	V,VI,VIII	LR-5	LARGE,MULTIPLE LOBULATED NODULES	YES	-	WASHOUT	WASH OUT	-	0	0	0	0	O	0	0	0	0
1	3	860820	V/VIII	LR-5	6.7X6.6	YES	-	WASHOUT	WASH OUT	0	0	0	0	0	0	0	0	0	0
1	4	392419	VI&VII	LR-TIV	12.1X6.2X10.4	YES	-	WASHOUT	WASH OUT	0	0	0	0	0	0	0	0	0	0
1	5	1322924	VII/VI	LR-5	6.9X5.8X7	YES	-	WASHOUT	WASH OUT	0	0	0	0	0	0	0	0	0	0
1	6	1324104	VIII,V,I	LR-5	8X7.6X8.3	YES	-	WASHOUT	WASH OUT	0	0	0	0	0	0	0	0	0	0
1	7	1286987	II	LR-5	7X3.5X3.4	YES	-	WASHOUT	WASH OUT	0	1	VIII/V	LR-5	5.2X2.7	YES	WASHOUT	WASHOUT	1	VI
1	8	1097131	VI	LR-5	5.6X7	YES	-	WASHOUT	WASH OUT	0	1	VIII/V	LR-5	2.9X2.5	YES	WASHOUT	WASHOUT	1	IVa
1	9	641416	VI	LR-5	5.5X3.3X5.0	YES	-	WASHOUT	WASH OUT	0	0	0	0	0	0	0	0	0	0
1	10	869663	VI	LR-5	4.1X2.8	YES	-	WASHOUT	WASH OUT	0	1	IV	LR-5	1.7X1.4	YES	WASHOUT	WASHOUT	1	VII
1	11	546458	VIII	LR-5	5.3X5.3	YES	-	WASHOUT	WASH OUT	0	0	0	0	0	0	0	0	0	0
1	12	407857	VI	LR-5	3.7X3.0	YES	-	WASHOUT	WASH OUT	0	1	VIII	LR-3	0	0	0	0	0	0
1	13	924473	VII	LR-5	2.8X2.6	YES	-	WASHOUT	WASH OUT	0	1	II	LR-4	2.1X2.3	YES	NO	NO	0	0
2	1	1188711	VI	LR-5	5.0 X 5.0	YES	WASHOUT	WASHOUT	-	0	0	0	0	0	0	0	0	0	0
2	2	29233	VIII	LR-5	1.1 X 1.3	YES	WASHOUT	WASHOUT	-	0	0	0	0	0	0	0	0	0	0
2	3	428361	VIII	LR-5	1.5 X 1.2	YES	WASHOUT	WASHOUT	-	0	1	VI	LR-4	0.8 X 0.8	YES	WASHOUT	WASHOUT	0	0
2	4	1138000	VI	LR-5	3.0 X 2.8	YES	WASHOUT	WASHOUT	-	0	0	0	0	0	0	0	0	0	0
2	5	50336	IV B	LR-5	1.3 X 1.3	YES	WASHOUT	WASHOUT	-	0	0	0	0	0	0	0	0	0	0
2	6	1140560	VII	LR-5	4.9 X 4.8	YES	WASHOUT	WASHOUT	-	0	0	0	0	0	0	0	0	0	0
2	7	234553	II/III	LR-5	3.4 X 3.1	YES	WASHOUT	WASHOUT	-	0	0	0	0	0	0	0	0	0	0
2	8	940257	VI	LR-5	3.2 X 3.0	YES	WASHOUT	WASHOUT	-	0	1	II	LR-4	2.3 X 2.0	YES	NO	NO	1	VI

								FOLLOW UP 6 WEEKS(BLUE COLOR LESION1,YELLOW COLOR LESION 2, GREEN COLOR LESION 3)									
TACE1/MWA.2	**S.No**	**MRD**	**LESION 3-LR**	**LESION 3-SIZE-CM**	**LESION 3-APHE**	**LESION 3-PORTAL**	**LESION 3-VENOUS**	**TOTAL NO.OF LESIONS AFTER 6 WEEKS**	**COUINAUD SEGMENTS-FOR LESIONS 6 WEEKS**	**LR(LESION 1)**	**LR LESION-1 6WEEKS**	**LESION 1-SIZE**	**LR (LESION 2)**	**LR LESION-2,6WEEKS**	**LESION 2-SIZE**	**LESION 3-SIZE**	**LR, LESION-3, 6 WEEKS**
1	1	858846	LR-3	6MM	YES	NO WASH OUT	NO WASH OUT	2	VIII,III	LR-5 LR-TRV(VIABLE-SEG VIII)	LR-TR VIABLE	1.2X0.7 CM	LR -4(SEG-III)	LR-4	.8X.7	0	0
1	2	763086	0	0	0	0	0	1	V,VI, VIII	LR-TRV(VIABLE)	LR-TR VIABLE	LARGE	0	0	0	0	0
1	3	860820	0	0	0	0	0	1-HCC, 4 BENIGN	VII	LR-4(SEG V/VIII)	LR-4	10X8MM	LR-5(SEG VII) **NEW LESION**, L LOBE	LR-5 NEW LESION	11X8MM	3LESIONS , L LOBE	LR-3, 3 LESIONS
1	4	392419	0	0	0	0	0	0	0	LRTR-NON VIABLE	LR-TR NON VIABLE	0	0	0	0	0	0
1	5	1322924	0	0	0	0	0	1	VII,VI	LRTR-VIABLE(VII/VI)	LR-TR VIABLE	6.3X6.1X6.8	0	0	0	0	0
1	6	1324104	0	0	0	0	0	1	V,VIII	LRTR-VIABLE(V,VIII)	LR-TR VIABLE	3.2X1.7	0	0	0	0	0
1	7	1286987	LR-5	2.1X1.8	YES	WASH OUT	WASH OUT	0	0	LRTR-NON VIABLE(SEGII	LR-TR NON VIABLE	6X5CM	LRTR-NON VIABLE(SEGVII	LR-TR NON VIABLE	-	1X7CM	LR-TR NONVIABLE
1	8	1097131	LR-5	1.0X1.0	YES	WASH OUT	WASH OUT	**3**	V,V/VIII, IV a	LRTR-VIABLE(SEG V)	LR-TR VIABLE	4.9X4.7CM	V/VIII LRTR-VIABLE	LR-TR VIABLE	3.3X3.5CM	IVa , 1.0X1.0	LR-TR VIABLE
1	9	641416	0	0	0	0	0	1	VI	LRTR-VIABLE(SEG VI)	LR-TR VIABLE	2.4x3.2 CM	0	0	0	0	0
1	10	869663	LR-5	1.3	YES	WASH OUT	WASH OUT	3	VI,IVa,VII	LRTR VIABLE(SEG VI)	LR-TR VIABLE	2.5X2.3	IVa, LR-VIABLE, LR-5	LR-TR VIABLE	2.3X2.1CM	VII,1.3CM	LR-TR VIABLE
1	11	546458	0	0	0	0	0	1	VIII	LRTR VIABLE(SEG VIII)	LR-TR VIABLE	2.6X1.3CM	0	0	0	0	0
1	12	407857	0	0	0	0	0	1	VI	LR-5,(SEG VI	LR-TR VIABLE	4.5X4.1	0	0	0	0	0
1	13	924473	0	0	0	0	0	1	VII	LR-5,(SEG VII	LR-TR VIABLE	3X2.8 CM	0	0	0	0	0
2	1	1188711	0	0	0	0	0	0	0	0	0	-	0	0	0	-	0
2	2	29233	0	0	0	0	0	1	-	LR-TR VIABLE	LR-TR VIABLE	-	0	0	0	-	0
2	3	428361	0	0	0	0	0	0	0	LR-TR EQUIVOCAL	LR-TR EQUIVOCAL	-	LR-TR NONVIABLE	LR-TR NON VIABLE	0	-	0
2	4	1138000	0	0	0	0	0	0	0	LR-TR NON VIABLE	LR-TR NON VIABLE	-	0	0	0	-	0
2	5	50336	0	0	0	0	0	0	0	LR-TR NON VIABLE	LR-TR NON VIABLE	-	0	0	0	-	0
2	6	1140560	0	0	0	0	0	0	0	LR-TR NON VIABLE	LR-TR NON VIABLE	-	0	0	0	-	0
2	7	234553	0	0	0	0	0	0	0	LR-TR NONVIABLE	LR-TR NONVIABLE	-	0	0	0	-	0
2	8	940257	LR-5	2.8 X 2.3	YES	WASHOUT	WASHOUT	2	-	LR-TR NONVIABLE	LR-TR NONVIABLE	-	LR-TR VIABLE	LR-TR VIABLE	-	-	LR-TR VIABLE

				FOLLOW UP 3 MONTHS(BLUE COLOR LESION1,YELLOW COLOR LESION 2, GREEN COLOR LESION 3)								FOLLOW UP 1 YEAR(BLUE COLOR LESION1,YELLOW COLOR LESION 2, GREEN COLOR LESION 3)					
TACE1/MWA.2	**S.No**	**MRD**	**LESION 3-LR**	**TOTAL NO.OF LESIONS AFTER 3 MONTHS**	**COUINAUD SEGMENTS- FOR LESIONS 3 MONTHS**	**F/U 3 M, LESION 1 SEGMENT**	**LESION 1 , 3M, SIZE**	**LESION 1-LR**	**LESION 2-LR**	**LESION 3, SEGMENT**	**LR LESION 3**	**TOTAL NO.OF LESIONS AFTER 1 YR**	**COUINAUD SEGMENTS- FOR LESIONS 1 YR**	**F/U-1 YR, LESION 1, SIZE**	**LESION 1**	**LESION 2**	**LESION 3**
1	1	858846	0	0	0	-	-	LR-TR NONVIABLE	LR-III	-	0	3	VIII,V, III,	2.9X2.2	2.9X2.2,SEGM VIII LR-VIABLE	3.4X1.8,SEG V, LR-5, NEW	13MM,SEG III,LR-5
1	2	763086	0	0	0	-	-	0	0	-	0	0	0	-	0	0	0
1	3	860820	LR-3, 14X11 MM	0	0	-	-	0	0	-	0	0	0	-	0	0	0
1	4	392419	0	0	0	-	-	0	0	-	0	-	-	-	LR-TR-NON VIABLE	0	0
1	5	1322924	0	0	0	-	-	0	0	-	0	0	0	-	0	0	0
1	6	1324104	0	0	0	-	-	0	0	-	0	0	0	-	0	0	0
1	7	1286987	LRTR-NON VIABLE(SEGVII	0	0	-	-	0	0	-	0	0	0	-	0	0	0
1	8	1097131	LRTR-VIABLE(SEG IVa)	-	IVa	-	-	0	0	Iva	**NEW**	0	0	-	0	0	0
1	9	641416	0	0	0	-	-	0	0	-	0	0	0	-	0	0	0
1	10	869663	LR-5	0	0	-	-	0	0	-	0	1	VIII	-	LR TR VIABLE(VIII), **NEW LESION** LR-5(II)	0	0
1	11	546458	0	0	0	-	-	0	0	-	0	1	VIII	4.2X4.1	LR-TR VIABLE	0	0
1	12	407857	0	2	VI, IV/V	VI	4.5X4.1	LR-TR VIABLE	NEW MULTIPLE LESIONS RT LOBE	-	0	0	0	-	0	0	0
1	13	924473	0	0	0	-	-	0	0	-	0	0	0	-	0	0	0
2	1	1188711	0	0	0	-	-	0	0	-	0	0	0	-	0	0	0
2	2	29233	0	1	-	-	-	LR-TR VIABLE	0	-	0	0	0	-	0	0	0
2	3	428361	0	0	0	-	-	LR-TR NONVIABLE	LR-TR NONVIABLE	-	0	0	0	-	0	0	0
2	4	1138000	0	0	0	-	-	LR-TR NONVIABLE	0	-	0	0	0	-	0	0	0
2	5	50336	0	0	0	-	-	LR-TR NONVIABLE	0	-	0	0	0	-	0	0	0
2	6	1140560	0	0	0	-	-	LR-TR NONVIABLE	0	-	0	0	0	-	0	0	0
2	7	234553	0	0	0	-	-	LR-TR NONVIABLE	0	-	0	0	0	-	0	0	0
2	8	940257	LR-TR VIABLE	1	-	-	-	LR-TR NONVIABLE	LR-TR VIABLE	-	LR-TR VIABLE	0	0	-	0	0	0

			m RECIST													
TACE1/MWA.2	S.No	MRD	6WEEKS	3MONTHS	1YR	SURVIVAL	NEW LESIONS	F/U MONTHS	CAUSE OF DEATH	CT. FINDING	LIVER	CIRRH.SIZE, SPLEEN	SURFACE NODULARITY	RECANULIZATION OF UMBILICAL VEIN	RX, STRATEGY	DOXORUBICIN
1	1	858846	PR	CR	PD	LOST F/U	NEW LESION, 1 YEAR	24	-	CIRRHOSIS, PHT,	DYSMORPHIC	12.2	NODULAR	NO	HEPAsphere	NO
1	2	763086	PD	PD	0	DEATH	-	<6M0NTHS	METASTASIS (VERTEBRA), DECOMPENSATED CIRRHOSIS	CIRRHOSIS	DYSMORPHIC	13.1	NODULAR	NO	LIPIODOL	YES,75 MG
1	3	860820	PD	PD	0	YES	NEW LESION , 6 WEEKS	>6M	-	CIRRHOSIS	DYSMORPHIC	14	IRREGULAR	YES	LIPIODOL	YES, 75MG
1	4	392419	CR	CR	CR	YES	-	12	-	CLD, HCC,CHOLILITHIASIS	DYSMORPHIC	13	NODULAR	NO	LIPIODOL	NO
1	5	1322924	SD	SD	SD	YES	-	12	-	CIRRHOSIS, PHT,	DYSMORPHIC	27	IRREGULAR	NO	TACE	NO
1	6	1324104	SD	SD	0	YES	-	>6M	-	CLD,PHT	DYSMORPHIC	19.1	IRREGULAR	NO	TACE	NO
1	7	1286987	CR	CR	CR	YES	-	>1YR	-	CLD	DYSMORPHIC	14.4	IRREGULAR	NO	HEPAsphere,LIPIDOL	YES, 75MG
1	8	1097131	PD	PD	0	DEATH	IVa, NEW-3MONTHS	6M	DECOMPENSATED CIRRHOSIS	CIRRHOSIS, PHT,	DYSMORPHIC	12.5	IRREGULAR	NO	HEPAsphere,LIPIDOL	YES,75 MG
1	9	641416	SD	SD	0	LOST F/U	-	6M	-	CLD, PHT	2.4X3.2CM	17.5	NORMAL	NO	TACE	NO
1	10	869663	SD	SD	0	DEATH	NEW LESION LR-5(SEG II)-1 YEAR	<6M	DECOMPENSATED CIRRHOSIS	CIRRHOSIS, PHT,	DYSMORPHIC	15.6	NODULAR	NO	HEPAsphere	YES,75 MG
1	11	546458	PR	PD	PD	YES	NEW MULTIPLE LESIONS RT LOBE	> 1 YR	-	CIRRHOSIS, PHT,	NORMAL SIZE, DYSMORPHIC	17.5	IRREGULAR	NO	DC BEADS	YES, 75 MG
1	12	407857	PD	PD	0	DEATH	-	6M	DECOMPENSATED CIRRHOSIS	CIRRHOSIS, PHT,	DYSMORPHIC	14	IRREGULAR	YES	TACE	NO
1	13	924473	PD	PD	0	DEATH	THROMBOSIS IVC, PUL METASTASIS	6M	PUL METASTASIS, DECOMPENSATED CIRRHOSIS	CLD, PHT,VASC INVASION	DYSMORPHIC	16.8	NODULAR	NO	TACE	NO
2	1	1188711	0	0	0	DEATH	bleed in post-ablation cavity	-	-	-	-	-	-	-	-	-
2	2	29233	PD	PD	0	YES	2 new lesions at 6 weeks	-	-	-	-	-	-	-	-	-
2	3	428361	CR	CR	-	YES	-	-	-	-	-	-	-	-	-	-
2	4	1138000	CR	CR	-	YES	-	-	-	-	-	-	-	-	-	-
2	5	50336	CR	CR	-	YES	-	-	-	-	-	-	-	-	-	-
2	6	1140560	CR	CR	-	YES	-	-	-	-	-	-	-	-	-	-
2	7	234553	CR	CR	-	YES	-	-	-	-	-	-	-	-	-	-
2	8	940257	SD	SD	-	YES	-	-	-	-	-	-	-	-	-	-

TACE1/MWA.2	S.No	MRD	Initials	Age	Sex	BASIC DIAGNOSIS	IF CIRRHOSIS: RISK FACTORS	ASCITIS	ENCEPHALOPATHY	VIRAL LOAD	ANTI.VIRAL RX	VIRAL STATUS	ALCOHOL	SMOKER	OPIUM	PRESENTATION	FH. CIRRHOSIS	T. BILIRUBIN	D. BILIRUBIN	IND. BILIRUBIN
2	9	1162884	BS	63	M	CIRRHOSIS	ALCOHOL	YES	NO	NO	NIL	ABSENT	YES	NO	NO	INCIDENTAL	NO	2.07	1.39	0.6
2	10	1145734	RK	62	M	CIRRHOSIS	ALCOHOL	YES	NO	NO	NIL	ABSENT	YES	NO	NO	INCIDENTAL	NO	0.84	0.17	0.7
2	11	1236781	AS	46	M	CIRRHOSIS	ALCOHOL	NO	NO	NO	NIL	ABSENT	YES	YES	YES	INCIDENTAL	NO	1.26	0.61	0.5
2	12	217864	RK	63	M	CIRRHOSIS	HCV	NO	NO	NO	ON TREATMENT	ABSENT	NO	NO	NO	SURVEILLANCE	NO	2.21	0.57	0.5
2	13	1076314	SRG	81	F	CLD	NASH	NO	NO	NO	NIL	ABSENT	NO	NO	NO	SURVEILLANCE	NO	0.2	0.06	0.9
2	14	966261	GR	60	M	CIRRHOSIS	ALCOHOL	NO	NO	NO	NIL	ABSENT	YES	YES	NO	INCIDENTAL	NO	1.21	0.81	3.1
2	15	334842	SS	54	M	CIRRHOSIS	NASH	YES	NO	NO	COMPLETED	ABSENT	NO	NO	NO	SURVEILLANCE	NO	0.53	0.25	3

TACE1/MWA.2	S.No	MRD	SGOT	SGPT	T. ALBUMIN	T. PROTEIN	ALK PHOS	HB	WBC	PLT	PT/INR	S. CREAT	S. UREA	AFP.	CHILD-PUGH	MELD	BCLC	L LOBE HYPERTROPHY	VASCULAR THROMBOSIS	METASTASIS	ANY COLLATERAL	TOTAL NO.OF LESIONS BEFORE RX	COUINAUD SEGMENTS-FOR LESIONS BEFORE RX	NO OF LESION
2	9	1162884	79	42	3.49	6.9	92	11	3.6	80	1.41	0.74	20	.	CLASS A	13	STAGE B	NO	NO	NO	NO	1	VIII	1
2	10	1145734	37	16	3.87	7.5	320	9.4	3.1	98	1.21	1.28	39	.	CLASS A	9	STAGE B	NO	NO	NO	NO	3	VI/VII, VIII,VIII	1
2	11	1236781	54	44	3.7	8.1	97	13	7.9	120	1.23	0.82	20	12.09	CLASS A	10	STAGE B	YES	NO	NO	NO	2	I,VI	1
2	12	217864	47	42	2.7	5.7	380	13	5.8	97	1.21	0.45	20	193	CLASS B	12	STAGE B	NO	NO	NO	NO	1	VIII	1
2	13	1076314	40	20	3.5	6.8	69	11	7.4	189	1.28	0.83	31	-	CLASS A	9	STAGE B	NO	NO	NO	NO	1	IV	1
2	14	966261	45	48	3.4	6.8	90	8.5	2	50	1.3	1.17	28	-	CLASS A	12	STAGE A	NO	NO	NO	NO	1	VII	1
2	15	334842	156	87	3.8	6.3	205	9.8	5.2	62	1.09	0.95	31	-	CLASS B	7	STAGE B	YES	NO	NO	NO	2	VIII	1

			BEFORE TREATMENT(BLUE COLOR LESION1,YELLOW COLOR LESION 2, GREEN COLOR LESION 3)															
TACE1/MWA.2	S.No	MRD	LESION 1-COUINAUD. SEGMENT	LESION 1-LR	LESION 1-SIZE, CM	LESION 1-APHE	LESION 1-PORTAL	LESION 1-VENOUS	LESION 1-DELAYED PHASE	LESION 1-FNAC/BX	LESION 2-NO OF LESION	LESION 2-COUINAUD.SEGMENT	LESION 2-LR	LESION 2-SIZE, CM	LESION 2-APHE	LESION 2-PORTAL	LESION 2-VENOUS	LESION 3-NO OF LESION	LESION 3-COUINAUD.SEGMENT
2	9	1162884	VIII	LR-5	4.0 X 3.8	YES	WASHOUT	WASHOUT	-	0	0	0	0	0	0	0	0	0	0
2	10	1145734	VI/VII	LR-5	1.7 X 1.4	YES	WASHOUT	WASHOUT	-	0	1	VIII	LR-5	3.1 X 2.4	YES	WASHOUT	WASHOUT	1	VIII
2	11	1236781	I	LR-5	2.0 X 1.7	YES	WASHOUT	WASHOUT	-	0	1	VI	LR-5	1.3 X 0.8	YES	WASHOUT	WASHOUT	0	0
2	12	217864	VIII	LR-5	4.9 X 4.7	YES	WASHOUT	WASHOUT	-	0	0	0	0	0	0	0	0	0	0
2	13	1076314	IV	LR-5	5.0 X 4.8	YES	WASHOUT	WASHOUT	-	0	0	0	0	0	0	0	0	0	0
2	14	966261	VII	LR-5	1.6 X 1.6	YES	WASHOUT	WASHOUT	-	0	0	0	0	0	0	0	0	0	0
2	15	334842	VIII	LR-5	2.3 X 2.0	YES	WASHOUT	WASHOUT	-	0	0	0	0	0	0	0	0	0	0

								FOLLOW UP 6 WEEKS(BLUE COLOR LESION1,YELLOW COLOR LESION 2, GREEN COLOR LESION 3)									
TACE1/MWA.2	S.No	MRD	LESION 3-LR	LESION 3-SIZE-CM	LESION 3-APHE	LESION 3-PORTAL	LESION 3-VENOUS	TOTAL NO.OF LESIONS AFTER 6 WEEKS	COUINAUD SEGMENTS-FOR LESIONS 6 WEEKS	LR(LESION 1)	LR LESION-1 6WEEKS	LESION 1-SIZE	LR (LESION 2)	LR LESION-2,6WEEKS	LESION 2-SIZE	LESION 3-SIZE	LR, LESION-3, 6 WEEKS
2	9	1162884	0	0	0	0	0	0	0	LR-TR NONVIABLE	LR-TR NONVIABLE	-	0	0	0	-	0
2	10	1145734	LR-5	3.4 X 2.9	YES	WASHOUT	WASHOUT	0	0	LR-TR NONVIABLE	LR-TR NONVIABLE	-	LR-TR NONVIABLE	LR-TR NON VIABLE	0	-	LR-TR NONVIABLE
2	11	1236781	0	0	0	0	0	0	0	LT-TR NONVIABLE	LT-TR NONVIABLE	-	LR-TR NONVIABLE	LR-TR NON VIABLE	0	-	0
2	12	217864	0	0	0	0	0	0	0	LT-TR NONVIABLE	LT-TR NONVIABLE	-	0	0	0	-	0
2	13	1076314	0	0	0	0	0	0	0	LR-TR NONVIABLE	LR-TR NONVIABLE	-	0	0	0	-	0
2	14	966261	0	0	0	0	0	0	0	LR-TR NONVIABLE	LR-TR NONVIABLE	-	0	0	0	-	0
2	15	334842	0	0	0	0	0	0	0	LR-TR NONVIABLE	LR-TR NONVIABLE	-	0	0	0	-	0

				FOLLOW UP 3 MONTHS(BLUE COLOR LESION1,YELLOW COLOR LESION 2, GREEN COLOR LESION 3)								FOLLOW UP 1 YEAR(BLUE COLOR LESION1,YELLOW COLOR LESION 2, GREEN COLOR LESION 3)					
TACE1/MWA.2	S.No	MRD	LESION 3-LR	TOTAL NO.OF LESIONS AFTER 3 MONTHS	COUINAUD SEGMENTS- FOR LESIONS 3 MONTHS	F/U 3 M, LESION 1 SEGMENT	LESION 1 , 3M, SIZE	LESION 1-LR	LESION 2-LR	LESION 3, SEGMENT	LR LESION 3	TOTAL NO.OF LESIONS AFTER 1 YR	COUINAUD SEGMENTS- FOR LESIONS 1 YR	F/U-1 YR, LESION 1, SIZE	LESION 1	LESION 2	LESION 3
2	9	1162884	0	0	0	-	-	LR-TR NONVIABLE	0	-	0	0	0	-	0	0	0
2	10	1145734	LR-TR NONVIABLE	0	0	-	-	LR-TR NONVIABLE	LR-TR NONVIABLE	-	LR-TR NONVIABLE	0	0	-	0	0	0
2	11	1236781	0	0	0	-	-	LR-TR NONVIABLE	LR-TR NONVIABLE	-	0	0	0	-	0	0	0
2	12	217864	0	0	0	-	-	LT-TR NONVIABLE	0	-	0	0	0	-	0	0	0
2	13	1076314	0	0	0	-	-	LT-TR NONVIABLE	0	-	0	0	0	-	0	0	0
2	14	966261	0	0	0	-	-	LR-TR NONVIABLE	0	-	0	0	0	-	0	0	0
2	15	334842	0	0	0	-	-	LR-TR NONVIABLE	0	-	0	0	0	-	0	0	0

			m RECIST													
TACE1/MWA.2	S.No	MRD	6WEEKS	3MONTHS	1YR	SURVIVAL	NEW LESIONS	F/U MONTHS	CAUSE OF DEATH	CT. FINDING	LIVER	CIRRH.SIZE, SPLEEN	SURFACE NODULARITY	RECANULIZATION OF UMBILICAL VEIN	RX, STRATEGY	DOXORUBICIN
2	9	1162884	CR	CR	-	YES	-	-	-	-	-	-	-	-	-	-
2	10	1145734	CR	CR	-	YES	-	-	-	-	-	-	-	-	-	-
2	11	1236781	PD	PD	-	YES	new lesion in seg VIII at 6 weeks and multiple at 3 months	-	-	-	-	-	-	-	-	-
2	12	217864	CR	CR	-	YES	-	-	-	-	-	-	-	-	-	-
2	13	1076314	CR	CR	-	YES	-	-	-	-	-	-	-	-	-	-
2	14	966261	CR	PD	-	YES	one new lesion at 3 months	-	-	-	-	-	-	-	-	-
2	15	334842	CR	PD	-	YES	one new lesion at 3 months	-	-	-	-	-	-	-	-	-

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The Principal,
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Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 31.08.2018 has approved the plan of thesis of Philipose Puliyelil Abraham, a student of your college for **MD Radio-diagnosis** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
Evaluation of the role of locoregional interventional therapies in the treatment of hepatocellular carcinoma

Supervisor
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The student may submit the four copies of thesis, to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She may be directed to attach a photocopy of this letter with the forwarding letter while submitting thesis in the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic, if any.

SP Singh
Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

1. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*
2. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

EVALUATION OF THE ROLE OF LOCOREGIONAL INTERVENTIONAL THERAPIES IN THE TREATMENT OF HEPATOCELLULAR CARCINOMA

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN

PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

In

RADIODIAGNOSIS

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

JANUARY, 2018

DR. PHILIPOSE PULIYELIL ABRAHAM

DEPARTMENT OF RADIODIAGNOSIS
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	Evaluation of the Role of Locoregional Interventional Therapies in the Treatment of Hepatocellular Carcinoma
For the degree of	MD (Radiodiagnosis)
Name of the candidate	Dr. Philipose Puliyelil Abraham
Supervisor	Dr. Siddharth Prakash
Co-supervisor(s)	Dr. Ajit Sood, Professor & Head, Department of Gastroenterology, DMCH, Ludhiana Dr. Archana Ahluwalia, Professor, Department of Radiodiagnosis, DMCH, Ludhiana
Institution	Dayanand Medical College and Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction:

Hepatocellular carcinoma (HCC) is the 5th most common neoplasm worldwide and the 3rd most common cause of cancer related death. It mainly affects patients of cirrhosis of any etiology.

Treatment options include for HCC include surgery - resection or transplantation, locoregional interventional therapies which include percutaneous ablative therapies and transarterial therapies and systemic therapy.

Aim of Study:

To evaluate the role of locoregional interventional therapies in patients of Hepatocellular carcinoma presenting to the Department of Radiodiagnosis in Dayanand Medical College and Hospital, Ludhiana prospectively over a period of 1 year and retrospectively over a period of 2 years and their outcomes according to the mRECIST criteria.

Materials & methods:

The locoregional interventional therapies for HCC included in this study are, Percutaneous ethanol injection (PEI), Radiofrequency thermal ablation (RFA), Microwave thermal ablation (MA), Trans-arterial radioembolization (TARE) and Trans-arterial chemoembolization (TACE).

In this study shall follow patients of Hepatocellular carcinoma presenting to the Department of Radiodiagnosis in Dayanand Medical College and Hospital, Ludhiana during a period of 1 year prospectively and 2 years retrospectively, who undergo Locoregional interventional therapies for treatment of HCC, with the intention to cure, downstage or provide palliative care.

Clinical Significance:

Many patients of HCC at presentation are not viable candidates for surgical resection or liver transplantation. Locoregional interventional therapies provides these patients and their treating physicians an alternative to systemic therapy alone for their management.

Keywords:

Hepatocellular carcinoma; Ablative therapy; Radiotherapy; Transarterial chemoembolization; Transarterial radioembolization; Radiofrequency thermal ablation; Microwave thermal ablation; Percutaneous Ethanol Injection

(Signature) Candidate	(Signature) Co-supervisor	(Signature) Co-supervisor	(Signature) Supervisor	(Signature) Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled "EVALUATION OF THE ROLE OF LOCOREGIONAL INTERVENTIONAL THERAPIES IN THE TREATMENT OF HEPATOCELLULAR CARCINOMA" exist in the Department of Radiodiagnosis, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate herself under our supervision and guidance.

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BY
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2. HOD Surgery	2. HOD Pathology
3. HOD Pathology	3. HOD Pharmacology
4. HOD Medicine	4. HOD SPM
5. Dean Academics	5. HOD Medicine
6. Vice Principal	6. HOD Surgery
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Approved: Yes / No

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Approved: Yes / No

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Ethics Committee

Chairperson
Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

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4	DATE OF ADMISSION OF COURSE	31st May 2017
5	TITLE OF THE TOPIC	Evaluation of the role of locoregional interventional therapies in the treatment of hepatocellular carcinoma

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Hepatocellular carcinoma (HCC) is the 5th most common neoplasm worldwide and the 3rd most common cause of cancer related death, mainly affecting patients of cirrhosis of any etiology.[1] Most HCC is thought to be associated with either chronic hepatitis C virus (HCV) or hepatitis B virus (HBV) infection and alcohol abuse.

Among patients with localized stage HCC, treatment options include resection or transplantation. Surgical resection is still considered the best therapy for HCC but is generally reserved for patients with solitary tumors with preserved liver function – preserved liver function being defined as absence of clinically relevant portal hypertension (i.e. hepatic venous gradient of less than 10mmHg, absence of varices splenomegaly and a platelet count of more than 100000/mm3) and normal bilirubin levels.[1]

However, many patients at presentation have unresectable disease, the overall resectability rate for HCC being only about 10-25%, and even among those that undergo surgical resection there is a recurrence rate of up to 80% at 5 years.[2]

When patients are unsuitable for resection they may be considered for liver transplantation or can be treated with percutaneous ablation therapy Liver transplantation is an effective intervention for HCC patients with cirrhosis since it removes the tumor itself as well as replaces the cirrhotic liver. Optimal candidates for liver transplantation are patients with single HCC of size less than 5cm or with 3 or less than 3 nodules less than 3 cm, without extrahepatic or vascular spread.[1] However, use of this modality is challenged greatly due

to the of availability of donor livers and tumor progression and death during the wait period.

With the advent of locoregional therapies there opens new possibilities for the treatment for patients of HCC. Locoregional therapies are now widely considered for use as bridge therapies in patients of early or intermediate HCC and in some patients of advanced HCC.[3]

Percutaneous ablative therapies are a viable option in patients which present with solitary nodule less than 5cm or up to 3 nodules less than 3cm, showing promising results and also in such tumors that are deemed unresectable due to higher disease burden and comorbidities.

When diagnosed at an intermediate, stage if the patient is still asymptomatic and has satisfactory hepatic reserve, chemoembolization can be considered being is reported to improve survival in well-selected patients with unresectable HCC. Many patients who are diagnosed with HCC however have advanced disease and are only candidates for palliative care.[1]

In this study we will follow patients of HCC for who, after through discussion between their consulting physician and interventional radiologist regarding their treatment options, undergo locoregional interventional therapy for treatment of HCC, with the intention to cure, downstage or provide palliative care.

The procedures performed at Dayanand medical college and hospital and included in this study are Percutaneous ethanol injection (PEI), Radiofrequency thermal ablation (RFA), Microwave thermal ablation (MA), Trans-arterial chemoembolization (TACE) using DEB-TACE or HepaSphere-TACE and Trans-arterial radioembolization (TARE) using SIR-Spheres.

Although in most studies the approach to the treatment of patients of HCC is designated by grouping into various staging systems, the most commonly used of which being the BCLC staging system, in many cases depending on available clinical resources, patient resources and the opinion from thorough discussion between the treating consultant physician and interventional radiologist, an approach is decided upon, the fundamental aim being to prolong the life of the patient and minimize suffering.

6.2 REVIEW OF LITERATURE

A meta-analysis by Orlando et al. published in 2009 in the American journal of gastroenterology looked to compare PEI and RFA in the treatment of small HCC - Small HCC being defined as solitary HCC < 5 cm or with up to 3 nodules smaller than 3cm, according to the Milano criteria. The study incorporated 5 RCTs and included a total of 701 patients, 354 of which were treated with RFA and 347 treated with PEI.

The results of the meta-analysis showed that in patients with small HCC the treatment with RFA is superior to treatment with PEI. Treatment with RFA is correlated to a better overall survival, survival at 1, 2, and 3 years, and cancer-free survival at 1, 2, and 3 years and tumor response. It also concluded that patients treated with RFA have a much lower risk of local recurrence.

One of the trials however showed nearly equivalent survival with the two treatments; but in this study the number of patients with Child-Pugh class B cirrhosis was distinctively higher than in the other trials and there was no correlation between the rate of tumor response and the survival rate. The findings of this one study likely indicate that patients in Child – Pugh A class are the better candidates for RFA.[4]

A study conducted by Shibata et al published in 2002 compared the treatment of small HCC, in this study being defined as a solitary HCC nodule smaller than 4 cm in diameter or those with two or three nodules less than or equal to 3 cm in diameter, by RFA and MA. This study included 72 patients with 94 HCC nodules, randomly assigning them for treatment either by to RFA or MA

groups. 36 patients with 48 nodules were treated with RFA, and 36 patients with 46 nodules were treated with MA.

They found that the number of treatment sessions per nodule in the RFA group was considerably lower than that in the MA group, the multiple sessions of MA required to cause complete nodule necrosis meant a prolonged treatment source as compared to RFA. While the mean time required for an individual MA session (33minutes +\-11), was significantly shorter than that required for an RFA session (53 minutes +/ - 16).

It also showed that there was no significant difference in the rate of complete therapeutic effect between the two groups; 96% for RFA and 89% for MA; P=0.26.

The rates of residual foci of untreated disease in RFA group and MA group were 4% and 10% and after 1 year 12% and 24% respectively. At 2 years there was no significant difference in the rates of residual foci of untreated disease between the two groups however those that underwent RFA showed a lower rate of complications.[5]

In 2011 Salem et al published a comparative effectiveness analysis of TACE and TARE therapies in patients with HCC. Using the collected data, over a 9-year period from 463 patients who were treated with either chemo-embolization or radioembolization. After eliminating patients who were not appropriate for comparison, the data from a total of 245 patients - 122 who received chemoembolization and 123 who received radioembolization was used.

They concluded that patients with HCC treated by chemoembolization and radioembolization with Yttrium-90 microspheres displayed similar survival

times. Radioembolization however resulted in longer time to progression of the tumor and displayed less toxicity than chemoembolization. Time to progression, as defined in the NCI Dictionary of cancer terms, being the length of time from the date of diagnosis or start of treatment for a disease until the disease starts getting worse or spread to other parts of the body.

A Post hoc analysis of sample size indicated that to attempt to establish an equivalence of survival times that an RCT would require a sample size of >1000, as such though there are ongoing RCTs with transarterial locoregional therapies none use overall survival as the primary end point due to this statistical barrier to demonstrating equivalence.[6]

A similar study by Laura E. Moreno-Luna et al published in 2013 in the journal of Cardiovascular and Interventional Radiology compared the efficacy and safety of TARE versus TACE in patients of HCC. This study took included patients of HCC deemed not to be candidates for orthotopic liver transplant, surgical resection or local ablation and were given treatment either with TARE or TACE. Those included in the study were similar in age, sex and degree of liver function based on MELD score. The study included only patients with patent portal veins – as TARE is often indicated in patients with occlusive portal vein thrombosis whereas TACE is contraindicated, thereby matching patients treated with TACE and TARE for equivalent severity of disease.

The study found that survival rates and response to treatment were quite similar in both groups. As for side effects, fever was significantly greater in those treated with TACE while fatigue was the major side effect seen in those patients treated with TARE. Due to its minimal side effects TARE can be performed as an outpatient procedure with virtually all patients meeting the

criteria for discharge on the day of the procedure while TACE requires as least overnight hospitalization – with around 20% of patients included in the study requiring >2 days of hospitalization after TACE for management of side effects. In terms of the number of treatments performed, 72% of patients treated with TARE required only a single treatment with TARE compared to 40% of patients that were treated with TACE, with 60% of patients treated with TACE requiring multiple treatments.

11% of patients treated with TARE were subsequently treated with TACE – this was done when a patient had received the maximum amount of radiation they can receive by TARE or when a patient had a relatively limited disease in the second lobe of liver which can be treated with limited subselective administration of TACE. TARE however is not usually performed after TACE as TACE is embolic, precluding effective delivery of the radioactive microspheres used in TARE.

In conclusion the study found that both treatments had similar treatment response, overall survival and side effect profile and TARE appears to be a promising treatment option in the treatment of unresectable HCC.

Evidence of the safety and efficacy of TARE from reports of both single-center and multicenter observational cohorts is promising however, due to the lack of randomized control study data supporting the efficacy and safety of TARE over TACE the AASLD (American Association for the Study of Liver Diseases), EASL (European Association for the Study of the Liver), and European Organization for Research and Treatment of Cancer do not currently endorse TARE as a standard treatment for HCC. For the same reason TARE is not recommended in the current BCLC staging system.

Hence the need for more randomized controlled trials to confirm its clinical utility and to clearly define the populations in whom this treatment should be used.[7]

A meta-analysis conducted by J.B. Jia et al in 2017 compared RFA and resection in patients with HCC with Child-Pugh A liver cirrhosis – this was done in an effort to better balance patient groups, as comparison studies for resection and RFA becomes difficult due to selection bias, RFA being usually performed on patients with higher disease burden.

The study showed a better 3 year and 5 year overall survival and disease free survival for patients treated with resection. However, on further analysis it showed that in studies where the tumor was considered resectable and patients were not grouped according to baseline characteristics, resection did not show significantly improved 1 and 3 years overall survival and disease-free survival. It also found that no significant difference could be demonstrated in patients with tumors of less than or equal to 3cm and those limited to solitary tumors.

These findings suggest that in patients with tumors considered surgically resectable i.e. having good liver function and early-stage disease, resection and RFA have equivalent outcomes.[8]

A similar study by Yun Ku Cho et al published in 2011 in the journal of gastroenterology and hepatology compared RFA to surgical resection as primary treatment of hepatocellular carcinoma meeting the Milan criteria. It found that in patients receiving RFA versus patients receiving surgical resection as primary treatment options, in terms of overall survival a

statistically significant difference could not be demonstrated in the studies reviewed.

It also found that hepatic resection seems to be a better option for HCC >2cm than RFA as the rate of local recurrence in these cases were higher in patients treated with RFA. However, according the American association for the Study of Liver Diseases (AASLD) practice guidelines, hepatic resection is not recommended for the treatment of HCC when the expected operative mortality rate is greater than 3%. In these patients, other nonsurgical treatment options, such as local ablation therapies, may be considered as a primary treatment for HCC.

The study also suggested a modified protocol for the treatment of HCC meeting the Milan criteria, where both RFA and surgical resection can be considered as primary therapies, with rescue hepatic resection performed when an adequate safety margin is not achieved by primary RFA – as primary RFA does not hinder the performance of any additional rescue resections even in the case of local treatment failure.[9]

In a review and meta-analysis by Zheng Li et al published in the International Journal of Hypothermia in 2016, combination therapy of radiofrequency ablation and percutaneous ethanol injection versus monotherapy with radiofrequency ablation or percutaneous alcohol injection for HCC was analyzed to study its safety and efficacy. 13 studies were identified and used for this analysis including a total of 1621 patients.

The results of this study showed that RFA in comparison to PEI showed a significantly better overall survival, cancer free survival and complete tumor necrosis as well as a lower rate of local recurrence.

Comparison of RFA and PEI combination therapies with RFA alone showed that combination therapy was associated with an improved overall survival and significant reduction in local recurrence rate

The study concluded that combination therapy of RFA and PEI is more effective for the treatment of HCC than either of the therapies used alone.[10]

A review article by Dagmar Kollmann, Nazia Selzner and Markus Selzer published in Lagenbecks archives of surgery in 2017 looked into bridging therapy for patients of HCC awaiting liver transplant. In the review it is stated that about 20-30% of patients with HCC awaiting transplant will be removed from the list due to tumor progression and recommended that if a patient of HCC is expected to wait for more than 6 months for transplant they should be treated with a bridging therapy – these included locoregional interventional therapies, Radiotherapy/stereotactic body radiotherapy and systemic treatment. The decision on the therapy used as a bridging therapy in these patients depends mainly on the tumor size and number of lesions as well as liver function, with ablation being the preferred method for small tumors (<3cms) and TACE or TARE preferred in larger tumors and multiple lesions. Radiotherapy/stereotactic body radiotherapy can be used in patients with poor liver functions as a bridge therapy while the use of systemic chemotherapy as a bridge therapy, while has been shown to extend time to tumor progression currently lacks sufficient study and is not recommended as standard therapy.[11]

A similar study was done by Peiman Habibollahi et al published in 2017 in the journal of Cardiovascular and Interventional Radiology, wherein the impact of bridging therapies on survival in patients of HCC posted for liver transplant

was studied, with followup up to 6.5 years after the initial diagnosis of HCC. They found that in patients for which bridging locoregional therapies were given prior to orthotopic liver transplant the overall survival was slightly better – and though not statistically significant it was noted that those in the locoregional therapy group had a higher tumor burden based on different indices (such as largest tumor diameter, sum of largest tumor diameters, BCLC staging and Child Pugh score) and had spent a longer time on the wait list (median wait time of 4.4 months in the locoregional therapy group versus 1.8 months for the group that did not receive locoregional therapy) as well as having a lower dropout rate secondary to tumor progression.

This indicates that bridging locoregional therapies can extend the wait times for patients likely to be delisted due to tumor progression due to being close to the upper limits of the transplant criteria at the time of being listed for transplant.[12]

In a review by Ramanathan M: Seshadri et al published in the International Journal of the International Hepato-pancreato-Billiary Association in 2015, the outcomes of surgical resection and locoregional therapies were studied in patients with stage 3A HCC according to American Joint Committee on Cancer staging system (i.e. multiple tumors >5cm).

They concluded as per the cases studied that patients that underwent surgical resection had an overall survival of 26.6 months, those that received Locoregional interventional therapies 16.4 months and that those that received no treatment 4.8 months.

It was however observed that major surgical resection procedures such as lobectomy and trisectionectomy are reserved for patients with preserved liver

function and non-cirrhotic patients as these require hepatic venous occlusion and sometimes portal vein occlusion – patients of advanced stage HCC in the background of cirrhosis lack the synthetic reserve and are not considered ideal candidates for these procedures – these patients however can receive locoregional regional therapies such as TACE and thermal ablation in a palliative setting.

It was also found that in 189 patients included in the study for which data on the degree of fibrosis and cirrhosis was available the median survival for those patients with none-to-moderate degree of fibrosis was 35.8 months compared to 15.7 months in the severe-to-cirrhosis group. When compared to locoregional therapies in patients with severe fibrosis or cirrhosis who underwent surgical resection had a similar median survival – 15.3 months for Locoregional therapies and 15.7 months in surgical resection. This indicates that locoregional therapies in more advanced stages of fibrosis or cirrhosis have similar survival rates and can be offered when indicated.[13]

6.3 AIMS AND OBJECTIVES OF THE STUDY

To evaluate the role of locoregional interventional therapies in patients of Hepatocellular carcinoma presenting to the Department of Radiodiagnosis in Dayanand Medical College and Hospital, Ludhiana prospectively over a period of 1 year and retrospectively over a period of 2 years and to evaluate their outcomes according to the mRECIST criteria.

7. MATERIALS AND METHODS

7.1 Source of Data

The study will include diagnosed patients of HCC presenting to the Department of Radiodiagnosis in Dayanand Medical College and Hospital, Ludhiana prospectively for a period of 1 year from 1st Feb 2018 to 31st Jan 2019 and retrospectively for a period of 2 years from 1st Feb 2016 to 31st Jan 2018, who after thorough discussion of their case with their consulting physician and interventional radiologist regarding their treatment options, undergo locoregional interventional therapy for treatment of HCC, with the intention to cure, downstage or provide palliative care.

The study will be done after having taken informed consent from all prospective patients and using the data of previous patients treated for HCC using interventional therapies given that the data for patients included is complete and reliable.

The study will be done with the approval of the ethics committee.

Follow up of each patient will be considered for a period of 6 months; with 2 follow ups carried out at approximately 3 and 6 months after treatment is administered.

7.2 METHOD OF COLLECTION OF DATA

INCLUSION CRITERIA

Diagnosed patients of Hepatocellular carcinoma for which a locoregional interventional therapy for treatment of Hepatocellular carcinoma is done in accordance with the BCLC staging and treatment strategy for reference, with the intention to cure, downstage or provide palliative care.

EXCLUSION CRITERIA

1. Serum bilirubin >2
2. Main portal vein thrombus
3. Encephalopathy
4. Extrahepatic disease (unless extrahepatic sites are resectable or when there is palliative indication)
5. Thrombocytopenia or significant coagulopathy
6. Significant ascites
7. Insufficient data

Duration of study: 1 year prospectively and 2 years retrospectively

Treatment Strategies:

The Barcelona Clinic Liver cancer (BCLC) staging and treatment strategy is the most commonly used in our setting for reference to decide a treatment plan for a patient of HCC, being one of the more internationally accepted staging and treatment algorithms for HCC.

According BCLC strategy the indications of percutaneous ablation and TACE are as follows:

1. Percutaneous Ablation:
    a. BCLC Stage 0; Very Early stage
        i. Single nodule <2cm in size
        ii. Child-Pugh A with Performance status 0 with/without raised Portal venous pressure and Associated disease
    b. BCLC Stage A; Early stage
        i. Single or ≤3 nodules ≤3cm in size

i. Child-Pugh A-B with Performance status 0 with/without raised Portal venous pressure and Associated disease

2. TACE:

a. BCLC stage B; Intermediate stage

i. Large multinodular

ii. Child-Pugh A-B with Performance status 0

The Contraindications for these therapies would be:

a. BCLC stage C; Advanced stage

i. Portal invasion

ii. Extrahepatic spread

iii. Child-Pugh A-B with Performance status 1-2

b. BCLC stage C; Terminal stage

i. Child-Pugh C with Performance status of 3-4

TARE and Microwave ablation however are not specifically discussed in this treatment strategy. No distinctive study has been carried out in the Indian subcontinent to define a definitive treatment strategy for our population. As such the final treatment plan is a product of discussion between the gastroenterologist and interventional radiologist, a combination of their experience and expertise and studies carried out in the field; to define specific guidelines for the treatment strategy is therefore beyond the scope of this study with our current knowledge in this demographic, rather this study may serve to aid in improving our understanding of the treatment of HCC and its outcomes in the Indian demographic.

Combination therapies of TACE and TARE therapy are also practiced in some clinical settings and has been shown as an effective treatment modality particularly in patients with bilobar disease and may be used in certain patients if clinically indicated and considered the best course of action.

In patients of HCC with established cirrhosis severity of cirrhosis will be assessed using the Child-Pugh score and MELD score

The Interventional therapies for HCC included in the study and performed in Dayanand medial college and hospital are as follows:

1. Percutaneous ethanol injection (PEI)
2. Radiofrequency thermal ablation (RFA)
3. Microwave thermal ablation (MA)
4. Transarterial radioembolization (TARE) using SIR-Spheres
5. Transarterial chemoembolization (TACE) using DEB-TACE or HepaSphere-TACE

1. Percutaneous ethanol injection:

PEI is performed under Ultrasound guidance and under local anesthesia. In this procedure between 2 and 10ml of sterile absolute alcohol is injected into the tumor, this induces vascular thrombosis and coagulative necrosis. This method is rarely practiced now as newer modalities have developed. The most suitable patients are those with less than three small (<2 cm) tumors with good underlying liver function (Child's grade A)[2]

2. Radiofrequency thermal ablation (RFA):

In RFA, thermal ablation of tumor is achieved by oscillation of high-frequency (200–1,200 kHz) alternating electric current leading to agitation of local ionic milieu. This is done by creating closed-loop circuit, placing a

generator, large dispersive electrode (ground pad), a patient (resister), and a needle electrode in series. The agitation results in frictional heat around the electrode which can be controlled by modulation of the amount of radiofrequency energy deposited.[14]

Radiofrequency ablation is performed percutaneously under ultrasound guidance and short acting general anesthesia. A pre-incision is made and electrode needle is introduced under ultrasound guidance into the target lesion. The electrode needle is placed to expose a few centimeters of the tip of the electrode – usually the tip is placed at the bottom of the lesion about 0.5cm inside the tumor margin, and connected to the generator and the energy is started. Care must be taken to avoid close approximation of the electrode to any vessels before starting the generator.

3. Microwave Thermal Ablation (MA):

Microwave ablation refers to the use electromagnetic method for inducing tumor destruction by using devices of varying frequencies. For the performance of MWA the electrode is placed into the tumor from which an electromagnetic microwave is emitted with frequencies of at least 900 MHz. Different protocols for the temporal course of the energy are in use more commonly first the ablation is started with low energy, gradually increasing the power, while monitoring the ablation zone and watching for possible complications.[15,16]

Microwave ablation is performed percutaneously under ultrasound guidance and short acting general anesthesia. A pre-incision is made and electrode needle is introduced under ultrasound guidance into the target lesion. The electrode needle is placed to expose a few centimeters of the

tip of the electrode – usually the tip is placed at the bottom of the lesion about 0.5cm inside the tumor margin and connected to the microwave generator the energy is started.

4. Transarterial chemoembolization (TACE):

TACE combines transarterial delivery of chemotherapeutic agents into the tumor with embolization of the tumor vascularity. It is usually performed via the transfemoral route.[14]

Initially the patient is evaluated by triphasic CT to evaluate the tumor and the arterial supply of the tumor is mapped. The procedure is then performed by selective cannulation of the feeding arteries with a microcatheter via transfemoral route and then a chemoembolic mixture is infused into the feeding arteries. This is followed by embolization of the feeding arteries.

5. Transarterial radioembolization (TARE):

TARE combines a minimal embolic effect on tumor vascularity with cytotoxicity of radiation, using beta emitting radioactive element Yttrium containing microspheres, acting as brachytherapy. The preferential deposition of microspheres within the tumor allows selective irradiation of the target tumor rather than the normal hepatic parenchyma, thereby reducing the risk of radiation-induced liver disease.[14]

Initially the patient is evaluated by triphasic CT to evaluate the tumor and the arterial supply of the tumor is mapped. Radiolabeled albumin is injected into the lesion and perfusion scan is done to note the uptake of the radiolabeled albumin in the lesion and whether there is any leak of the material into adjacent structures. By selective cannulation, the feeding

arteries are chemoembolized and Yttrium containing microspheres are injected into the target area transabdominaly under ultrasound guidance.

STUDY DESIGN

The study is designed to be longitudinal and observational study including a combination prospective and retrospective patient data. The end point of the study being to evaluate the role of locoregional interventional therapies in the treatment of HCC in these patients and its outcome.

OUTCOME

Outcomes will be judged according to mRECIST criteria, the following definitions will be applied for tumor response to treatment:[17]

A. Complete response: (CR)

The disappearance of any intratumoral arterial enhancement in all target lesions

B. Partial response: (PR)

At least a 30% decrease in the sum of diameters of viable (contrast enhancement in the arterial phase) target lesions, taking as the reference the baseline sum of the diameters of target lesions

C. Progressive disease: (PD)

An increase of at least 20% in the sum of the diameters of viable (enhancing) target lesions, taking as the reference the smallest sum of the diameters of viable (enhancing) target lesions recorded since the treatment started

D. Stable disease: (SD)

Any cases that do not qualify for either partial response or progressive disease

Statistical Analysis

The relevant data will be collected and applicable tests applied. All statistical calculations will be done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

No.

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Attached herewith

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Performa for Locoregional therapies in HCC

Biodata:

Name-

Age - Sex –

MRD No.-

Contact No-

Address-

Clinical History

Basic diagnosis: normal liver cirrhosis CLD

IF Cirrhosis:

Etiology: HCV HBsAg Alcoholic NASH

Ascites: Yes / No

Encephalopathy: Yes / No

IF HCV/HbV +

Viral load

Genotype

Antiviral treatment: on treatment completed vaccinated

Viral status: response : present / absent

Alcohol: on / off

Smoker: Yes / No

Opium: Yes / No

Presentation : Incidental pickup surveillance decompensated cirrhosis

Family history of cirrhosis: Yes / No

Signature of Candidate

Signature of Supervisor

Investigations:

LFT

- T.Bilirubin
- Direct
- Indirect
- SGOT
- SGPT
- T.Albumin
- .T.Protiens
- Alk Phosphate

CBC

- Hb
- WBC
- Platelet

Coagulation Profile

- PT
- INR

RFT

- S.Cr
- Urea
- Na^+

AFP levels

CHILD Score

Meld Score

Signature of Candidate

Signature of Supervisor

CT Findings:

IF Cirrhosis

Size

Liver

Spleen

Surface: Nodular Irregular

Left lobe hypertrophy:

Recanalization of Umbilical vein:

Vascular Thrombosis

Main PV Rt branch Lt Branch

SMV

Any other

IVC

Metastasis:

Ascites:

SOL

Any Collateral

Lt Gastric

Short Gastric

Post gastric

Spleno-renal collateral

Signature of Candidate

Signature of Supervisor

Management:

BCLC Stage

Treatment Strategy

Any deviation from BCLC

Reason

Details of chosen strategy:

Alcohol ablation

TACE

Done with

GEL FOAM

DC BEADS Size

HEPAsphere size

Lipiodol Amount

Was gel foam used after particles

Amount of doxorubicin

RFA

Electrode size

Signature of Candidate

Signature of Supervisor

Was lesion close to vessel

Is lesion exophytic

Percutaneous balloon used

Where

Artificial ascites created

TARE

Volumetery

Rt lobe

Lt lobe

Tumor volume

Pre-procedure arteries embolized

Rt gastric

GDA

Collateral to tumor

Inf phrenic

L/Q scan

Dose

Post procedure L/Q scan

Signature of Candidate

Signature of Supervisor

	Lesion 1	Lesion 2	Lesion 3
Segment			
Size			
Arterial Enhancement			
Portal			
Venous			
Fnac/Biopsy			
Treatment Strategy			
F/u Imaging			

Signature of Candidate

Signature of Supervisor

Residual Lesion / Recurrence			
Further Tx			
F/u Imaging			
Resist Criteria (CR/PD/SD/PR)			

Signature of Candidate

Signature of Supervisor

Survival
Cause of Death

Signature of Candidate

Signature of Supervisor

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o..... .....am willing to participate in the study "EVALUATION OF THE ROLE OF LOCOREGIONAL INTERVENTIONAL THERAPIES IN THE TREATMENT OF HEPATOCELLULAR CARCINOMA" The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

....

Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____ _____

इस शोधकार्य "EVALUATION OF THE ROLE OF LOCOREGIONAL INTERVENTIONAL THERAPIES IN THE TREATMENT OF HEPATOCELLULAR CARCINOMA" में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫ਼ਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

"EVALUATION OF THE ROLE OF LOCOREGIONAL INTERVENTIONAL THERAPIES IN THE TREATMENT OF HEPATOCELLULAR CARCINOMA" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____
ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ

_____
ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____

ਮਿਤੀ_____

ਪਤਾ _____

ਪਤਾ _____

_____
ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____
ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ